THE ACUTE INFECTIOUS FEVERS

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AN INTRODUCTION FOR STUDENTS AND PRACTITIONERS

BY

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PREFACE

THIS work is based on the experience of teaching acute fevers in two medical centres London and Edinburgh During the time covered by that experience while considerable advances have been made in the field of infectious diseases it is interesting to reflect that in approaching the subject the medical student and the young resident medical officer continue to ask questions which fundamentally remain very much the same An endeavour has been made in this work to provide answers to these questions Whilst it would be too much to expect that those with great experience of the subject would agree with all the views expressed the latter at least ought to form a reasonable guide for the beginner until adequate observation has enabled him to form his own opinions There are few aspects of the diseases dealt with in which the author has not had a good deal of personal experience and he has firmly resisted the temptation to write on subjects not covered by this It is to be hoped therefore that the work will be found useful to students junior medical officers in hospital and practitioners who wish to brush up their knowledge of common conditions

For their kindness in permitting the use of illustrations and other material thanks are due to the following —Sir W W Jameson Chief Medical Officer to the Ministry of Health formerly Dean of the London School of Hygiene and Tropical Diseases Professor Drennan of the Pathology Department University of Edinburgh the Editors of the Lancet and British Medical Journal Dr Hubert Smith formerly of the Shanghai Municipal Council Drs A B Donald and Scott Forrest senior assistants at the Edinburgh City Hospital and The Genito Urinary Manufacturing Company

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CHAPTER I

SCARLET FEVER

Synonym—Scarlatina

Pathology The work of the Dicks (1923) and Dochez (1924) pointed almost conclusively to the streptococcus pyogenes as the cause of scarlet fever and the evidence in favour of this organism may be summarised as follows —

1 Streptococcus pyogenes can be recovered from over 90 per cent of cases of scarlet fever in the acute eruptive stage and the disease has been reproduced in susceptible human subjects by swabbing the throat with the organism

2 The organism produces a soluble exotoxin which in human susceptibles provokes a skin reaction known as the Dick test and fails in those who are immune Thus in a large proportion of cases of scarlet fever in the earliest stages of the disea e the Dick test is positive and becomes negative in convalescence The toxin is neutralised *in vitro* by the serum of scarlet fever convalescents

3 In response to toxin injections the horse elaborates an antitoxin which neutrali es the toxin *in vitro* gives the Schultz Charlton blanching effect in scarlet fever rashes produces a passive immunity to scarlet fever as measured by its action in protecting exposed susceptibles and by the Dick test and has a specific therapeutic effect when injected in the early days of the disease Injection of the toxin into human subjects may produce a reaction indistinguishable from the toxæmia of a mild attack of scarlet fever and by suitably grading the doses of toxin an active immunity to scarlet fever is induced

Whilst the organism is often referred to as a hæmolytic streptococcus on account of one of its most striking cultural characteristics when grown on fresh blood agar all attempts to show a specific relationship between any particular type or

strain of this organism and scarlet fever have failed By Lancefield s (1933) precipitation method streptococci from cases of scarlet fever can be shown to fall into Group A a group containing streptococci pathogenic for the human subject Griffith (1935) by specific agglutination reactions subdivided the streptococci concerned in the production of human disease into approximately forty individual types and was of the opinion that these constituted a bacterial species which he designated streptococcus pyogenes His method of typing enabled him to observe the clinical results of the spread of infection by individual types in various communities and to show that such diver e clinical manifestations of infec tion as scarlet fever tonsillitis erysipelas and puerperal sepsis may result from infection by the same serological type About twenty of these types appear to be epidemiologically significant and in England scarlet fever is due mainly to types 1 and 2 In view of these and numerous observations by other workers a profound change in our outlook on the epidemiology of scarlet fever has been brought about Scarlet fever can no longer be regarded as forming an epidemiological entity but as only one clinical manifestation of epidemic streptococcal infection

The pathological conception of the disease attributes *toxigenic* and *pyogenic* functions to the organism When clinical infec tion occurs the streptococcus produces inflammatory changes at the site of implantation usually the fauces and naso pharynx and in addition a soluble exotoxin which by diffusion into the blood stream causes a generalised toxemia exemplified by such features as rash and tachycardia At any stage including convalescence the pyogenic function of the organism may be displayed by the occurrence of septic complications *e g* adenitis or otitis media Usually the organism remains in the nasopharynx or those structures which it can reach by the lymphatics draining that region and it is only occasionally found in the blood stream or in remote tissues On post mortem examination apart from such lesions as nasopharyn gitis middle ear suppuration or its complications or the usual pathological features of acute nephritis or broncho pneumonia there are no characteristic changes indicative of scarlet fever

Two specific immunity reactions occurring in the human

subject are found in scarlet fever the Dick test and the Schultz Charlton phenomenon

The *Dick Test* is a test for susceptibility to scarlet fever and is elicited by the intradermal injection of 0 1 or 0 2 c c of a suitable dilution of toxin selected by a process of trial and error in human subjects from a strain of streptococcus pyo genes It is usually performed on the flexor surface of the left forearm and controlled in the other arm by a similar injection of toxin inactivated by heat In susceptibles including a varying proportion of cases of scarlet fever in the first two or three days of illness a circumscribed patch of erythema 10–40 mm in diameter appears at the site of injection in about six hours and reaches its maximum in from twelve to twenty four hours It disappears in two or three days Pseudo reactions probably due to sensitivity to the heat stable fraction of the bacterial protein described by Ando Kurauchi and Nishimura (1930) resulting in a transient erythema at the control site are not numerous In natural immunes and the majority of convalescent cases of scarlet fever no reaction appears The test occasionally gives anomalous results for example scarlet fever occurs now and then in Dick negatives Fraser (1937) explaining these by his finding that there are certain differences within the group of erythrogenic toxins so that an antitoxic immunity against the preponderance of these would not necessarily be valid against all These differences however as far as practical experience goes must be few and such occasional anomalies do not impair the general usefulness of the test Its introduction has enabled the immunity of large numbers of the population to be estimated In New York Zingher (1924) demonstrated that skin sensitivity to the toxin increases from the fifth or sixth month of life onward and is greatest at the one to two year age period when over 70 per cent of children may be expected to be susceptible Thereafter susceptibility decreases until at the age of twenty and over the percentage of positives falls to about 18 per cent The same observer found that susceptibility varies according to social and environmental circumstances positive reactors being much more common in children of well to do parents than in those from less fortunate homes and in those from rural as compared with urban communities

The *Schultz Charlton* reaction takes its name from the two workers who first noted (1918) that serum from certain individuals when *injected intradermally into the skin of a patient* with a scarlatinal rash caused the disappearance of the rash over the area of skin infiltrated by the serum Mair (1936) suggested that this was a specific reaction only given by the serum of patients immune to scarlet fever and we have seen that the production of the reaction by the injection of serum from horses immunised by the exotoxin of streptococcus pyogenes forms one of the important steps in the proof of the specific relationship between that organism and scarlet fever In practice the phenomenon usually described as blanching or extinction is now elicited by the intradermal injection of 0 2 to 0 5 c c of scarlet fever antitoxin into an area of skin on which the rash is well marked Blanching when it appears does so in from six to eighteen hours after performing the test the amount varying from complete local disappearance of the rash to slight fading (See Fig 2 facing page 8)

Generally blanching outlasts the fading of the rash on the rest of the body and only infrequently is the blanched area invaded by the exanthem Desquamation also may be inhibited over that area Occasionally blanching may be masked in individuals sensitive to serum by a local erythema due to serum proteins The value of the test in diagnosis is discussed in the section dealing with that subject

Etiology Geographically scarlet fever finds its main distribution in the temperate and colder zones of Europe America Asia and Australia its occurrence in the tropics being rare In Great Britain it is most prevalent from August to November but the numbers attacked vary widely from year to year periods of unusually high incidence recurring at intervals of from five to seven years The age incidence is mainly in school children those between five and six years suffering most heavily whilst in infants under one year the disease is unusual In respect of sex incidence females are more often attacked than males Fatal cases are most likely to occur in those under five years Historically scarlet fever has exhibited well marked fluctuations in severity and according to Greenwood (1935) has appeared in specially severe epidemic form in England certainly twice and probably

three times within the limits of modern history The present epidemic type in Western Europe and America is mild with a case fatality rate of under 1 per cent In England and Wales this is the sequel to a decline in scarlet fever mortality which set in about the seventies of last century and which has been progressively maintained till the present In Eastern Europe and the Far East however scarlet fever still maintains its severity and produces fatality rates of 10 to 15 per cent or more

Transmission The fact has already been referred to that according to modern conceptions of the epidemiology of scarlet fever this disease can only be regarded as one clinical manifestation of epidemic streptococcal disease Sources of infection must therefore include any patent infection by streptococcus pyogenes particularly of the upper respiratory tract as well as typical and atypical cases of scarlet fever They must also include contact carriers in the general population and convalescent carriers who continue to harbour the organism for varying periods after recovery from scarlet fever tonsillitis and other infections Spread occurs by direct contact and droplet infection the organism being contained in nasopharyngeal secretions and suppurative discharges from the nose ear or glands Indirect spread may be by manual transmission the hands having been contaminated by droplet or suppurative discharges whilst the use of infected cups spoons and instruments *e g* clinical thermometers are also obvious means of dissemination Milk is also a well recognised vehicle of infection having been infected by human agency at some stage before it reaches the consumer or as Minett (1937) suggests by udder infection of human origin in the cow Its derivative ice cream has also been incriminated With the widespread introduction of efficient pasteurisation however milk outbreaks have become less common Since Chapin (1910) emphasised the importance of droplet and manual transmission of the causal agent of scarlet fever epidemiologists have been inclined to attach little importance to fomites such as infected books and to dust Evidence has been forthcoming however that the streptococcus may remain viable when separated from the human host and investigators such as Allison (1938) have resuscitated the doctrine that infection by dry dust

particles or particles in the air is by no means impossible The site of implantation of the organism in the great majority of cases is in the nasopharynx although in surgical scarlet fever it gains access to a raw surface or through an abrasion in the skin or mucous membrane

Infectivity Scarlet fever is a disea e of moderate infectivity if we restrict the term infection to mean case infection with the disease It is a matter of common observation that it does not spread with the same facility as for example measles and chickenpox when introduced into a children s ward and when necessary the disease can be safely nursed by barrier or bed isolation methods The patient is probably capable of trans mitting infection from the moment the organism gains a footing in his tissues and certainly from the time of appearance of the first symptom There is evidence that infectivity persists longer in children under five years than in others and in those who contract the disease in the winter months but practical experience teaches that uncomplicated cases are not likely to infect others at the end of the fourth week of the disease and most fever hospitals recognise this by discharging such cases at the end of this period The presence of desquamation is not now regarded as evidence *per se* of infectivity Those who develop catarrhal or suppurative discharges are deemed infectious until these have ceased Bacteriological standards of freedom from infectivity have not so far been generally recommended

Incubation and Quarantine Period The incubation period is usually short from one to four days but maximal periods of eight to ten days have been reported A quarantine period of seven days will be found adequate as a routine measure and certain authorities are content to observe a period of five days

Clinical Features The stage of invasion in scarlet fever commonly lasts from one to three days but occasionally the period which elapses between the first symptom and the efflorescence of the rash is prolonged for nearly a weel In mild cases it may be entirely absent the first indication of the disease being slight malaise and the rash but even in these there is usually some complaint of sore throat Well-defined cases show a sudden onset with sore throat headache and

nausea or vomiting These symptoms are accompanied by a rise in temperature to 100 or 101 F but temperatures of 102 or 103 F are not uncommon The pulse rate is increased out of proportion to the pyrexia and may be 130 or 140 In sharp cases the patient is flushed and restless or delirious he may *complain of generalised aching or even pains in various joints* vomiting may be persistent and diarrhœa occasionally occurs Examination of the throat at this stage reveals the usual signs of an acute pharyngitis and tonsillitis while occasionally acute otitis media may have made its appearance

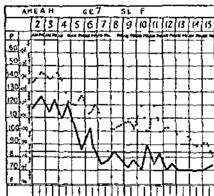


Fig 1 Temperature and pulse chart of typical case of scarlatina simplex not treated with serum Note rapid lysis

Stage of Eruption When the rash comes out the condition becomes recognisable as scarlet fever and the eruptive stage lasts about five days The temperature is at its height when the rash is fully developed anything between 100 and 104 F and unless an early complication supervenes it falls by rapid lysis to normal with the fading of the rash The tachycardia is maintained during the early stages of the rash but the pulse resumes its normal rate with the fall in temperature In appearance the patient is flushed and the eyes clear although in sharp cases the conjunctivæ tend to show a pinky tinge A circumoral pallor is often well defined

Throat There is always some degree of faucial inflammation but in mild cases this is not prominent the patient complaining of nothing more than dryness of the throat and on examination there is only slight injection of the fauces and soft palate with or without slight enlargement of the tonsils In severe cases the tonsils are greatly swollen almost meeting in the mid line the whole of the fauces soft palate uvula and post pharyngeal wall being intensely congested Faucial œdema is well marked and swallowing attended with discomfort and

pain sometimes described as radiating to the ears Occasionally thick speech and the characteristic bulging of the soft palate point in addition to peritonsillar inflammation Various types of exudate are seen on the tonsils in scarlet fever A follicular deposit is frequently found in other cases the tonsils are streaked with muco pus In a fair number of cases a membranous deposit is present and this is difficult to distinguish by clinical observation from diphtheritic membrane

Rash An enanthem may appear in the form of punctations on the soft palate even before and in the early eruptive stage but this is generally seen only in the well developed case The typical rash appears on the neck and the upper part of the chest and quickly spreads over the body and limbs A noteworthy point is that it avoids the face although in cases with bright rashes it may appear above the angle of the jaw In an average case the rash becomes sparse and fades out gradually below the elbows and knees In mild cases it may be limited entirely to the trunk whilst in sharp cases it may be distinct even on the palms of the hands and soles of the feet The rash in character is a punctate erythema consisting of innumerable scarlet pin points Its texture varies however from the homogeneous effect produced by the confluence of bright punctations giving the vivid boiled lobster appearance to the coarser type in which the individual puncta are almost macular in size Again on the forearms and legs *where the rash has become sparse on the extensor surfaces* it may assume a blotchy and pimply appearance Occasionally a miliary type of rash is seen In this the erythema is intense and punctations chiefly on the abdomen and chest show tiny vesicles in their centres In some situations the rash is better marked than in others and in faint faded rashes the best impression is usually obtained from the flanks back or inner surfaces of the thighs The rash disappears on pressure but in some instances petechiæ are noted below the clavicles on the anterior axillary fold and in the flexures of the elbows and groins According to its intensity the rash fades in three or four days or may persist for seven to eight days although the duration of a faint rash may be a matter of hours It becomes a dirty brownish tint before disappearing staining remaining in the flexures of the elbows abdomen and groins



Fig ~ Rash of scarlet f ver howing Schultz Cha lton blanching effect

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Fig. 3 Pinhole desquamation in axilla after scarlet fever



Fig. 4 Desquamation of hands in scarlet fever

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for a few days after the last traces have gone from the skin surface That scarlet fever may occur without the rash but with other characteristic manifestations including complications such as nephritis at the typical time as well as subsequent typical desquamation is undoubted but such cases must be very infrequent

Tongue During the first day or two the tongue is uniformly coated with a greyish white fur through which protrude the lingual papillæ—the white strawberry tongue The edges tips and surface along the median raphe then begin to peel and the fur disappears from before backwards leaving the tongue clean and beset with swollen papillæ The latter is the red strawberry tongue which may supply corroborative evidence in diagnosis though other conditions *e g* measles may give an appearance somewhat resembling it

Other Signs and Symptoms Varying with the severity of the faucial lesion there may be swelling and tenderness of the tonsillar glands The headache generalised aching and restlessness may continue into the eruptive stage and delirium if present may not abate until the temperature begins to settle Although occasionally the sharper form of the disease may be associated with diarrhœa constipation is the rule and the urine in addition to being highly coloured may show some degree of febrile albuminuria The characteristic odour of diacetic acid in the breath is readily noted in many patients

Stage of Desquamation and Convalescence Once the temperature is settled unless complications occur the progress of the patient is uneventful Strength gradually returns but in sharp cases it may be two or three weeks before weakness disappears

Desquamation This is the characteristic clinical feature of scarlet fever convalescence Its profusion and time of appearance are determined by the intensity of the rash bright rashes being succeeded by early and well marked desquamation while after less prominent eruptions it may be late in showing itself and rather scanty Exceptions to this rule however may disclose themselves well marked and even massive desquamation following rashes which have been quite unobtrusive It commences about the end of the first week with cracking and pinholing of the skin of the lobes of the ears and

the sides and root of the neck Small tags of superficial epider mis are detached, the surface presenting a roughened or ragged appearance From the neck the process spreads to the pectoral region and shoulders and occasionally to the pubic region It then progressively involves the trunk and the limbs About the end of the second week the skin of the fingers shows transverse cracking at the tips parallel to the free edges of the nails the process spreading over fingers and palms so that fairly large flakes are cast off Similar cracking at the toes is shown about the end of the third week, the tough skin of the heels being the last to be shed about the fifth or sixth week or later A wide variation in the amount and character of desquamation is found in individual patients and in slight attacks it may be absent or represented only by mild powdering the latter being the case especially in young children In rare instances the process may repeat itself after completion In sharp cases with intense rashes peeling may be so precipitate that the underlying new skin is tender and sensitive and owing to its flushed appearance has on occasion been mistaken for a recrudescence of the rash

Complications In the present epidemic type of scarlet fever with its low case fatality rate the complications of scarlet fever assume considerable importance since in them selves *e g* in the case of otitis media they may lead to chronic defects and either during the attack or at some remote period endanger life In a series of 1850 consecutive cases of scarlet fever admitted to the North Western Hospital London which were considered of insufficient initial severity to warrant serum treatment 33 per cent at all ages showed one or other of the common complications whilst in patients of five years or under 43 8 per cent were complicated The incidence of the common complications occurring singly or in conjunction with others was as follows arthritis 4 per cent adenitis after the first week 12 8 per cent otitis media 10 per cent rhinitis 20 per cent and nephritis 4 1 per cent From complications of the catarrhal or suppurative type strepto coccus pyogenes can almost invariably be isolated and in a proportion of cases the complication is undoubtedly the patho logical expression of the original infecting organism This however does not account for the complication in every case

as has been shown by Allison and Brown (1937) Using Griffith s method of typing they noted that complications occurring in patients in the third and subsequent weeks of scarlet fever treated in large wards were often due to sero logical types of cocci differing from those causing the original infection They attribute complications therefore in the majority of cases to re infection by strains from other patients a view which finds ready acceptance among many who had already arrived at similar conclusions as a result of their clinical observations The following is an account of the common complica tions of scarlet fever

Arthritis This may occur in three main forms in scarlet fever but an early toxic arthritis is by far the commonest and seems to be a specific manifestation of the disease It has a specially high incidence in adoles cent and young women and in those who have had a previous history of rhematism There is a remarkable constancy in the time of its occurrence the commonest days on which it appears being the seventh and sixth and over 60 per cent of the cases are seen between the fourth and ninth day The inflammatory process is found mainly in the periarticular tissues and some degree of myositis is associated with the arthritis pyrexia stiffness joint pains and swelling of the smaller joints are the usual signs the fingers and wrists being most liable to be affected although other joints such as the knees shoulders elbows and ankles are frequently implicated and indeed any joint in the body may be involved The condition is usually transient and clears up in a few days By far the greatest number of cases of arthritis in scarlet fever conform to the above type but occasionally another and much more serious variety occurs later in

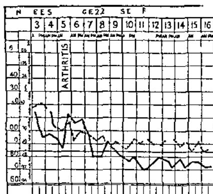


FIG 5 Temperature and pulse hart of case of early arthr t s of fingers wrists and shoulders Condition subsided with the temperatu e

convalescence about the third or fourth week which in its clinical manifestations is indistinguishable from acute rheumatism and is frequently associated with endocarditis Suppurative arthritis is an exceedingly rare complication of the present epidemic type of scarlet fever

Adenitis In the early eruptive stage some degree of cervical adenitis accompanies the faucial angina but complete or almost complete subsidence takes place as a rule by the end of the first week Later on however the complication may appear anew in convalescence or a sudden flare up may occur in a gland which has all but disappeared Children under five years of age are particularly liable to be affected and in the series quoted above 52 per cent of the cases occurred in this age group Whilst adenitis may occur occasionally in the submaxillary or sublingual glands it is almost invariably the tonsillar gland on one or both sides which becomes enlarged indurated and tender Swelling may appear very rapidly in fact quite a marked degree may come on overnight and from time to time an associated tonsillitis is found with the adenitis Even with considerable glandular enlargement pyrexia may be absent but as a rule temperature excursions are well marked and may be satisfactorily accounted for by even minor degrees of the complication General malaise may also be a feature of the condition Resolution usually occurs but in a proportion of cases suppuration results The lymph nodes along the line of the great vessels of the neck may rarely be involved and the inflammation spreading may give rise to cellulitis

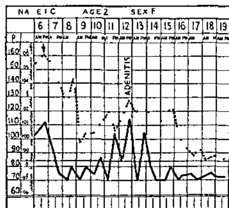


FIG 6 Temperature and pulse charts of a case of early cervical adenitis Patient received 3 c c refined scarlet fever antitoxin (↓) and a type 2 streptococcus was isolated from the throat on admission and when the adenitis was most pronounced The complication was only detected clinically on the twelfth day of illness

Otitis Media This most important complication may occur at any stage of scarlet fever including the stage of invasion and is found chiefly in patients under five In the series of cases at the North Western Hospital previously referred to 76 per cent of the patients developing otitis media fell into this age period Infection occurs by extension along the eustachian tube and the complication appears commonly in the first three weeks most frequently in the second It may disclose itself by pyrexia and earache direct examination of the drumhead revealing congestion and possibly bulging Swelling and tenderness of the lymph nodes over the tip of the mastoid may also be noted With the establishment of ear discharge either naturally or by surgical means pain and temperature subside In a great number of cases however estimated by W T Gardiner at two thirds in his series of cases the appearance of otorrhœa is unheralded by symptoms The condition usually clears up satisfactorily with conservative treatment but the possibility of mastoid extension should never be lost sight of especially as in small children this extension may be very insidious and even symptomless and a careful watch should be kept on the temperature and pulse rate Gardiner found mastoid involvement in 7 per cent of his otitis cases in Edinburgh whilst Abrams and Friedman (1933) quote as high a figure as 20 6 per cent for their cases in Boston These authorities discriminate between a more acute type in the first three weeks and a less acute and symptomless type after the fourth week Scarlatinal mastoiditis may lead to such further complications as lateral sinus thrombosis brain abscess and streptococcal meningitis

Rhinitis This commonly affects the younger patients and in the North Western series 67 per cent were under five years It occurs at an early stage in the disease and a large proportion of hospital cases are admitted with the complication Evidence of its occurrence is found in a thick muco purulent nasal discharge which may be very persistent The skin of the nostrils and lips may be reddened and excoriated and unless pre cautions are taken a purulent conjunctivitis may be set up Recurrences after apparent cessation are common especially if the patient contracts a common cold and since the nasal discharge is highly infectious a recrudescence of rhinorrhœa in

a patient whose isolation has recently been terminated is frequently responsible for the return case Although clinical signs of paranasal sinusitis only show themselves very infre quently Hoople and Cave (1933) are persuaded as a result of their radiological studies that some degree of this is the rule and may be regarded as part of the disease rather than a complication

Nephritis This is one of the characteristic complications of scarlet fever and is commonly of the glomerulo tubular type although an acute interstitial type has been described Its incidence varies in different epidemics and the North Western Hospital statistics show that it is slightly commoner in males than females It occurs with striking regularity at the end of the third week of the disease being often immediately preceded by a septic complication such as adenitis Irregular pyrexia headache nau ea and vomiting indicate the onset Œdema occurs early the face being pale and puffy and occasionally the hands feet and genitals show this feature al o Some degree of transitory hypertension is present and the output of urine is diminished The latter may vary in appearance from slightly smoky to dark brown or red owing to the presence of blood while microscopically red blood cells casts and epithelial *debris* are found In a fair number of cases the onset of the complication may be so insidious that the first warning of its presence is conveyed by albuminuria the presence of blood being delayed for a day or two As in a proportion of cases the urine shows nothing more than albuminuria when the ordinary chemical test is applied at the nephritic period it must be assumed that this is a manifestation of the same pathological proce s Recovery is the rule in from two to eight weeks but in severe cases uræmia with convulsions coma and hyperpyrexia may result in death Very rarely does the condition drag into the chronic stage before terminating fatally Ca es will be occasionally met with in which advice is sought for the first time on account of nephritis the patient or his relatives being unaware that he has had an attack of scarlet fever In these the as ociated desquamation usually gives the clue to the ætiology of the condition

Heart Complications There has been a good deal of dis cussion as to the role played by scarlet fever in the causation

of heart disease and as to the frequency of heart complications in scarlet fever In 24 012 cases of scarlet fever analysed in Edinburgh in 1924 we found endocarditis or pericarditis or both present in 0 25 per cent whilst in the more recent series of complications observed in the North Western Hospital not a single case occurred Nevertheless even with the present mild epidemic type of the disease endocarditis is occasionally encountered and we agree with Faulkner Place and Ohler (1935) that these cases are probably etiologically identical with the form of acute rheumatism seen after tonsillitis Whilst they may appear as early as the first or second week of

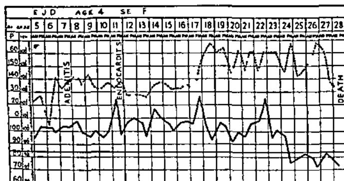


Fig 7 Temperature and pulse chart of fatal case of endocarditis occurring as a complication of scarlet fever Cervical adenitis appeared on the seventh day and by the eleventh day signs of endocarditis were unmistakable The cardiac lesion was rapidly progressive and patient died from congestive heart failure on the twenty-eighth day

the disease they are usually delayed till the third or fourth week and seem to have little relationship to the severity of the initial attack which may have been uncomplicated The onset is shown by a moderate rise in temperature with a rapid pulse and the patient looks really ill In the absence of obvious rheumatic pains other complications will usually be searched for in explanation of the fever but examination of the heart will usually disclose mitral endocarditis Whilst we have observed one or two cases which ran to a fatal termination in a few weeks usually with appropriate treatment the patients become afebrile and the condition quietens down Pericarditis may nowadays be regarded as a rare complication of scarlet fever

Other Complications Many other complications such as *boils abscesses* and *finger infections* may be found in con valescence *Tonsillitis* and *quinsy* may occur and *broncho pneumonia* may occasionally be set up after an acute naso pharyngitis when convalescence has apparently been estab lished *Pleurisy with effusion* and *empyema* appears to be much less common than in the past *Vulvovaginitis* due to streptococcus pyogenes will be found in a small but definite proportion of little girls We have also noted one or two cases of *thrombo phlebitis* It should be noted that scarlet fever may be complicated by *encephalo myelitis* a condition which however seems to occur less often in this disease than in other common infections *e g* measles

Associated Diseases Scarlet fever convalescents seem to be specially susceptible to diphtheria usually in the form of anterior nasal diphtheria but the faucial and laryngeal types may also occur The co existence of scarlet fever and chicken pox has also attracted the attention of several observers as being more than a coincidence Scarlet fever convalescents al o occasionally contract erysipelas The relationship between scarlet fever and acute rheumatism has already been men tioned whilst erythema nodosum is occasionally found in the convalescence from scarlet fever

Relapse and Second Attack Relapse is a well recognised phenomenon in scarlet fever and in London and Edinburgh our annual rates have usually been in the neighbourhood of 2 per cent Anderson (1934) in Leeds reported a rate of 4 3 per cent and is of the opinion that this high incidence was due to the failure of the benign type of scarlet fever then prevailing to produce immunity Lichtenstein (1931) advanced a similar view when recording that mild epidemics are accompanied by a high and severe epidemics by a low relapse rate That this factor of immunity subsequent to attack is undoubtedly of importance has been confirmed by our own observations of patients in whom the persistence of a positive Dick reaction throughout convalescence was followed by relapse The work of Allison and Brown (1937) indicates that the streptococcus responsible for the secondary attack differs in serological type from the primary infecting organism When relapse appears it does so about the third or fourth week and displays the

usual clinical characteristics of scarlet fever Second attacks are also occasionally seen an interval of years having elapsed since the first In spite of the occurrence of relapses and second attacks it may be said that in the great preponderance of cases one attack of scarlet fever protects for life

Varieties of Scarlet Fever The description of scarlet fever previously given applies to all but a few cases of the disease and for this average type the term *scarlatina simplex* is employed Severe forms of the disease are sometimes encountered however and these are classified into *toxic* and *septic*

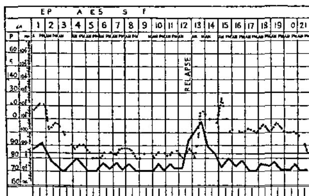


FIG 8 Temperature and pulse chart of relapse Note mild degree of pyrexia in initial attack

types Both are highly fatal but in recent years their virtual disappearance particularly in the case of the septic type has contributed materially to the fall in the scarlet fever case fatality rates which have been witnessed in this country since the war of 1914–18

Toxic Type The most prominent feature of this variety also known as *scarlatina maligna* is profound prostration The patient is limp cold and clammy the temperature high or hyperpyretic the pulse rapid and feeble whilst the throat may only present the signs of a mild angina or a follicular tonsillitis In some cases however faucial congestion is said to be intense and plum coloured The rash is ill developed or purplish in colour and in one recent case we have seen a typical scarlatiniform rash was replaced shortly before death

by a purpura involving nearly the whole of the skin surface of the body and limbs Continuous vomiting and diarrhœa are characteristic and before the introduction of specific treatment the condition was almost invariably fatal in one or two days Whilst complete exhaustion is usually a prominent feature some cases show an extreme degree of delirious excitement and may injure themselves or others in their maniacal outbursts In all cases death is due to circulatory failure and in the absence of distinctive signs during life the diagnosis is a

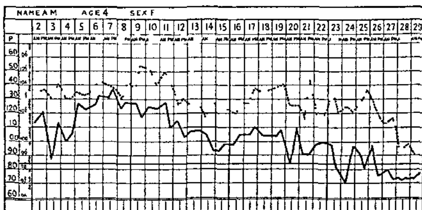


FIG 9 Temperature and pulse chart of recovered case of the septic type of scarlet fever Patient admitted with rash of moderate intensity and ulcerated throat Developed bull neck pouring nasal discharge and double otorrhœa by the eighth day Following doubl mastoidectomy on eleventh day gradually settled When discharged from hospital in twelfth week uvula practically disappeared and much destruction of soft palate

matter of considerable difficulty especially as post mortem examination shows nothing more than intense toxemic changes

Septic Type Also termed *scarlatina anginosa* this type is usually seen in young children and its clinical features appear to be the result of an exaggeration of the pyogenic properties of the infecting strain of streptococcus Throat signs and symptoms are severe from the first The rash is usually well developed but occasionally blotchy septic rashes especially in the neighbourhood of the large joints may confuse the appearance The temperature is high 103° or 104 F but

does not fall with the fading of the rash and a continuous fever is present until the issue is decided The septic process in the nasopharynx is very marked and the throat signs become worse ulceration giving rise to sloughs on the fauces tonsils and palate and eventually to partial destruction of one or other of these tissues The condition is very painful and the whole of the mouth and tongue becomes very dirty A continuous muco purulent discharge pours from the nose cervical adenitis results in bull necking and acute otitis media with its possible complications in the mastoid process and brain appears early Arthritis is common and broncho pneumonia a frequent complication The patient shows a hectic flush is miserable and restless and fights bitterly against all nursing attention If recovery ensues the temperature comes down gradually about the third or fourth week leaving the patient greatly exhausted so that convalescence is slow and often interrupted by bursts of pyrexia due to various complications Death may intervene at any stage from broncho pneumonia empyema or pericarditis suppurative complications involving the brain or meninges by way of the mastoid or ethmoid antra or occasionally from hæmorrhage following septic erosion of the great vessels of the neck

Other Varieties The terms *surgical* and *puerperal scarlet fever* are employed to designate certain forms of the disease but these are not special types in the sense of the term as employed in the foregoing and in fact the majority of such cases fall into the category of scarlatina simplex *Surgical scarlet fever* arises after burns and wounds in the skin or mucous membranes the causal organism being implanted on the injured tissues Except for the fact that faucial signs are mild or absent assuming that the site of implantation is not in the fauces as may occur after the surgical injuries resulting from tonsillectomy the disease pursues a normal course Probably the commonest forms of surgical scarlet fever apart from those occurring after burns are those following operations in the naso pharynx and its associated cavities chiefly tonsillectomy the onset of the disease occurring within the usual limits of the incubation period in the days immediately succeeding the operation *Puerperal scarlet fever* occurs during the puerperium and may be the result of infection occurring normally by

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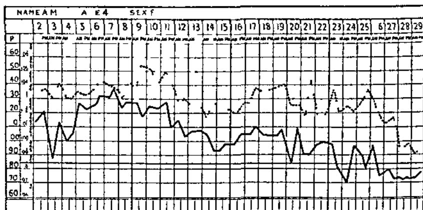


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by desquamation is however necessarily scarlet fever Desquamation commencing as pinholing on the neck or upper part of the chest and proceeding to cracking at the finger and toe tips at the appropriate period would be definite retrospective evidence of scarlet fever but in the difficult case more often than not such convincing evidence is absent or ambiguous and after weighing up all the factors diagnosis can only be a matter of probability The value of the *Dick test* in diagnosis is limited since all cases of scarlet fever do not give a positive result in the early stages whilst a fair proportion remain positive in convalescence The continuance therefore of a positive or a negative reaction from the earliest stages throughout convalescence would not rule out scarlet fever in the presence of characteristic clinical features but in their absence the diagnosis would be improbable The reversal of a Dick positive reaction in the early stages to a negative in convalescence during the course of an eruptive fever clinically suggestive of scarlet fever would be absolute confirmation of that diagnosis The *Schultz Charlton* reaction may also be of value but there are definite limits to its usefulness The absence of blanching does not in itself negative the diagnosis as Blake (1927) found that failure in 20 per cent of undoubted cases will occur and if the test is postponed until the third day of the rash in half the cases the phenomenon will not be elicited The reaction suffers somewhat also on account of its delay in time of appearance as by the time it may reasonably be expected to occur the background of rash may have faded In general therefore the results of this test in diagnosis are disappointing since it is in late faded rashes faint transient rashes or coarse equivocal rashes that assistance in diagnosis is most urgently required In actual practice the blanching effect is most consistent in the early typical punctate rash in which help in diagnosis is little needed and apart from its use in distinguishing between scarlet fever and rubella in which it may be helpful it is not much employed in routine work *Throat swabbing* may be of material assistance the presence of streptococcus pyogenes in nearly pure culture or in large numbers and particularly if these can be shown to belong to current epidemiological strains by serological typing giving support to the diagnosis Bearing in mind the frequency

invasion of the nasopharynx A certain proportion of these cases is however, really surgical scarlet fever the streptococcus pyogenes being implanted in the genital tract It has been stated that women in the puerperium are particularly prone to contract scarlet fever but Dick testing of such women does not show that they are more susceptible than others at the same age period Opinions differ as to the dangers of puerperal scarlet fever but since infection of the genital tract by streptococcus pyogenes always holds serious possibilities, caution should be observed in prognosis Even when the primary site of infection is in the fauces the most vigorous precautions are necessary to prevent transmission of the organism to the maternal passages

Typhoid Type This form of the disease has been described by Ker and Goodall among others but at present it is a rarity The condition commences as a well marked attack of scarlet fever but instead of the temperature subsiding with the abatement of the throat signs and fading of the rash it assumes a remittent character lasting for three or four weeks no complication being found to account for the pyrexia Exhaustion is also a feature

Diagnosis It has been questioned by Hobson (1936) whether the term scarlet fever has any claim to be retained in the clinician s vocabulary of diseases but our view at present is that while scarlet fever can no longer be held to be an epidemiological entity it must still be regarded as a clinical entity and as a descriptive term scarlet fever must still be retained Scarlet fever is a well recognised clinical combination of signs and symptoms and although from time to time one or other common feature may be absent diagnosis will depend very largely on the appearance of the throat and the rash particularly the latter In typical cases there will be little difficulty but if the rash has been faint or fleeting or if the case is seen when the rash has faded the only practical course is to isolate the patient and await events The cleaning of the tongue may be of assistance and the occurrence of such complications as early arthritis or nephritis at the characteristic time is very helpful Observation of a suspected case of scarlet fever however usually resolves itself into waiting for desquamation Not every case which has shown a suspicious erythema followed

or one or other of the barbiturates may bear a similarity to the scarlatinal exanthem *Serum rashes* are almost invariably urticarial in type and in our experience have not therefore given rise to much doubt in diagnosis and the same could be said of scarlatiniform rashes ascribed variously to septic processes articles of diet dentition enemata and purgatives On occasion however some forms of erythema the result of wearing a new garment next the skin have caused considerable uncertainty and it is possible that such rashes may be more frequent now than formerly owing to the sophistication of textiles The popularity of sunbathing has also been followed by erythemata and headache which the notifying practitioner has occasionally mistaken for scarlet fever *Exfoliative dermatitis* is also sometimes mistaken for scarlet fever in the stage of desquamation

Prognosis In the present epidemic type of the disease this is good the average case fatality rate in Great Britain being about 0 5 per cent With such a rate it is impossible to estimate the effect of the introduction of sulphonamides on the risk of death and the same will apply to penicillin when its use in scarlet fever becomes more general It is to the effect of these substances on complications that we have to look for an improvement in prognosis and whilst we believe that the outlook on these has improved with the use of sulphonamides it could hardly be said that this has been dramatic The introduction of the specific antitoxin has much improved prognosis in the toxic type of scarlet fever Whereas formerly practically every case succumbed a third or half of the patients may now be saved In the septic type prognosis still requires to be guarded antitoxin being able only to exert an uncertain effect on the septic processes associated with the upper respiratory tract but considerable benefit is to be expected from the use of sulphonamides and penicillin on this form of the disease Apart from the severe types prognosis depends on the occurrence of broncho pneumonia or otitis media followed by mastoiditis and brain complications such complications being the immediate cause of death in the few fatalities now encountered In uncomplicated otitis media satisfactory healing may be expected in a few weeks in the great majority of cases and in the past it has been customary to assume that hearing

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In differential diagnosis the appearance of the throat before the rash or after its disappearance may suggest *diphtheria* In the latter there is less redness of throat and palate membrane is more difficult to detach and the tongue does not undergo the characteristic changes seen in scarlet fever On clinical grounds however it is often a matter of the greatest difficulty to distinguish between membrane found in mild degrees of tonsillar diphtheria and some forms of streptococcal exudate including that found in scarlet fever and in these cases bacteriological examination in conjunction with Schick testing is of great assistance Apart from diphtheria the main difficulties arise in connection with other exanthemata and rashes following drugs enemata serum and various skin irritants *Rubella* when the rash is profuse and fine in texture on the trunk may resemble scarlet fever but its morbilliform appearance on the limbs *its presence on the face* the enlargement of the lymph nodes and catarrhal onset will usually decide The help which may be expected from the Schultz Charlton test in this connection has already been mentioned Prodromal rashes in *chickenpox* and *measles* not infrequently give occasion for errors in diagnosis as also do those of *smallpox* if that disease is prevalent In view of the resemblance which some chickenpox prodromal rashes bear to those of scarlet fever and the not infrequent concurrence of these diseases difficulties in the differential diagnosis are not uncommon and unless these are resolved by the appearance of blanching on performing the Schultz Charlton test often the only course is to await desquamation The prodromal scarlatiniform rash of measles also presents practical *difficulties especially as the rash* may be the most obvious of the early prodromal phenomena During measles epidemics the presence of catarrh in a suspected case of scarlet fever should engender caution and the appearance of Koplik s spots carefully watched for There should be no real difficulty in distinguishing between scarlet fever and measles during the stage at which the true rash of the latter is seen Of the *drug rashes* those due to belladonna aspirin

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is little if at all, affected subsequently Surveys by Kerridge (1937) among children in L C C special schools for the deaf with the gramophone audiometer however suggest that chronic hearing defects may be traced in about one sixth of cases to otitis media complicating the acute infectious diseases of childhood and in this group 22 per *cent were traced to scarlet* fever In view of these findings therefore it may be necessary to revise our views on prognosis in respect of hearing defects of which may only appear some time after discharge from hospital or isolation Nephritis must be taken seriously but in all but exceptional cases the immedate prognosis is good whilst the careful work of Campbell (1928) assures us that scarlet fever is not an important factor in the production of chronic nephritis in later life Endocarditis seems capable of showing a considerable degree of immediate recovery but if pericarditis occurs the outlook is very serious With reference to the effect of scarlet fever on patients already subject to rheumatic carditis we agree with Hector (1926) that there is a definite tendency towards an exacerbation of the heart lesion *which should be most carefully watched throughout the illness*

Prophylaxis General measures include compulsory notification with its administrative corollaries of hospital isolation and terminal disinfection of premises Whilst the facilities for treatment which exist in modern hospitals may possibly have made some contribution to the reduction of case fatality rates it is not now generally believed that hospital isolation has had much effect in preventing spread of infection The prevalence of a benign epidemic type of the disease has induced many public health authorities therefore to abandon wholesale hospital isolation in favour of home isolation in selected cases In some areas this policy has made little progress however as the general public having become accustomed to hospitalisation of scarlet fever *are difficult to convince that this is no* longer necessary Similarly views on terminal disinfection have undergone alteration and elaborate and expensive measures have been given up by many authorities and replaced by spring cleaning and thorough airing without detriment to the contacts Other administrative measures consist in imposing a quarantine period of seven to ten days on contacts and these are examined with a view to the discovery of a possible

infecting ambulatory case disclosed by the occurrence of desquamation or rhinorrhœa The milk supply is inquired into in order that this as a common factor in a series of cases may not escape attention Chiefly owing to the existence of large numbers of cases of latent and patent infection by streptococcus pyogenes especially in urban communities in which opportunities for frequent and intimate contact are many it is doubtful if these administrative measures apart from those directed to safeguarding the milk supply have more than a partial effect on the dissemination of scarlet fever even when pursued with exemplary thoroughness

Active Immunisation Streptococcal toxin has proved a relatively innocuous substance when inoculated into the human subject and since the discovery of the Dicks much work has been published on active immunisation which can now be regarded as a safe and reliable procedure In Western Europe and America probably owing to the mild type of scarlet fever now prevailing field work has not been pressed with the same energy as in the case of the corresponding procedure in diphtheria but in the Far East Toyoda (1930) has proved the value of active immunisation on a large scale In this country and America the method has been applied with a considerable amount of success to fever hospital staffs in whom the incidence of scarlet fever results in economic loss and disorganisation of training For example Benson (1928) in the Edinburgh City Hospital brought about a 91 per cent reduction in the incidence of scarlet fever among his nurses and at the North Western Hospital after the procedure was introduced scarlet fever was practically abolished from the nursing staff In practice individual immunity is estimated by the Dick test positive reactors receiving a course of five injections of 500 2 000 5 000 25 000 and 50 000 skin test doses[1] at weekly intervals The Dicks (1933) claim that with such a dosage 95 per cent of susceptibles will become Dick negative within two weeks after the final injection and it is to be expected that 90 per cent will remain immune for from one to five years As in all forms of active immunisation systemic reactions occur and

[1] The skin test dose is the amount of toxin necessary to produce a reaction at least 1 cm in diameter about twenty four hours after intracutaneous injection in the majority of individuals susceptible to scarlet fever

in Benson's series of young female adults these occurred in 10 per cent after one or other of the immunising injections When the initial immunising dose of 500 skin test doses is exceeded or in the highly susceptible the reaction occasionally reproduces the features of the initial toxemic phase of scarlet fever in a modified form with pyrexia malaise an enanthem and a scarlatiniform rash as its main characteristic To this the term scarlatinoid syndrome has been applied In order to save multiplying injections immunisation against scarlet fever and diphtheria may be combined the necessary doses of both antigens being mixed in the syringe before injection

Passive Immunisation As originally carried out the usual procedure was to Dick test the contacts and inject 5 to 10 c c of scarlet fever antitoxin *subcutaneously or intramuscularly* into contacts This gave immediate protection in a high percentage of cases in 84–95 per cent of cases in a series we reported in 1929 but the duration of immunity was relatively short and fell off rapidly after the first week To obtain immunity lasting for two or three weeks doses such as 10 c c *were necessary and in any case individuals showing a strongly* positive Dick test required that amount Since highly refined and concentrated scarlet fever antitoxin became available Bradshaw (1939) has reported that 0 75 c c of the serum will give a high proportion of successful passive immunisations in child contacts Experience has shown that passive immunisa*tion is only a partial remedy for the dropping cases which* are a problem to those in charge of residential schools children s wards etc since the effect seems to be in the nature of temporary blocking of the disease during which the tissues do nothing to clear themselves of the infecting agent When passive immunity has waned the invasive properties of the *organism assert themselves and the disease may occur* Employed therefore as the sole means of prevention it is apt to lead to a false sense of security which is dissipated by the appearance of further cases Accordingly the method has definite limitations but provided these are recognised it has certain spheres of usefulness *e g* in the prevention of scarlet *fever in susceptibles about to* undergo such operations in the nasopharynx as tonsillectomy

Treatment The patient should be isolated and whether

this is carried out in the home or the hospital will depend on the suitability of the home surroundings and the policy of the local public health authority If home isolation is decided on the requirements of the sick room in respect of good ventilation a sunny aspect an open fire and proximity to a water closet should be satisfied as far as possible The patient should have for his sole use and marked in some distinctive way if necessary crockery and cutlery tooth brush and hairbrush soap towels thermometer, and a supply of old books and toys which can be burned afterwards In the room should be placed two overalls just inside the door and a wash hand basin with soap nailbrush and some dilute disinfectant for the hands if desired The nurse or medical attendant must always put on the overall when entering the room and before leaving take it off and scrub up the hands With these precautions there need be no fear of the carriage of scarlet fever or other streptococcal infection from the patient to others A sheet wrung out in carbolic lotion 1 in 80 and hung over the doorway does nothing to prevent the spread of infection but is a useful warning to others to keep out Articles used for treatment or nursing should be sterilised at once—for example after food or medicine crockery should be boiled A plentiful supply of swabs to receive nasal discharges in the shape of cotton or linen rags or paper handkerchiefs should be provided and after use thrown at once in the fire After excreta have been deposited in the water closet bedpans should be wiped out with 1 in 20 carbolic lotion Bed and body linen can be dealt with safely in the domestic wash tub If home isolation is conscientiously carried out on these lines some medical officers of health for example Forrest (1936) have found no harmful results from allowing contacts to return to school or work after the expiry of the usual period of quarantine in the same way as if the patient had been removed to hospital It should be noted however in this connection that the official recommendation in the joint memorandum of the Ministry of Health and Board of Education is that school children living in the same house in which a patient suffering from scarlet fever is being treated should be excluded from school during the whole period of illness and for a week thereafter

The present day conception of the pathogenesis of scarlet

fever complications arising out of the work of Allison (1938) has introduced a number of problems into the methods of isolation and particularly the hospital management of patients *suffering from scarlet fever He found that complications* following re infection were frequent in multiple bed wards whereas in patients nursed in cubicles or in wards to which only patients with the same serological type of streptococcus were admitted they were few Allison recommends therefore cubicles for all cases of scarlet fever treated in hospital or their isolation in separate wards according to the serological type of primary infecting organism In passing it may be noted that the former of these recommendations gives strong support to the policy of home isolation As far as hospital isolation is concerned the structure of the majority of fever hospitals is hardly likely to permit individual isolation and consequently this proposal can only be regarded as a counsel of perfection Following the introduction of the doctrine of reinfection renewed consideration has been given to ward management and nursing methods with a view to preventing complications in open wards and undoubedly these can be reduced by attention to certain details In the first place unless the weather is too rigorous ventilation should approach *as nearly as possible to open air conditions Hospital practice* assumed in the past that in order to secure the well being of the patients scarlet fever wards should be maintained at a temperature of 60° F or over but this was too often realised at the expense of adequate ventilation The modern tendency is to make sure of ventilation and pay more attention to individual needs in respect of warmth the patient being kept comfortable in bed with hot water bottles garments and bed clothes In summer free use should be made of balconies Direct sunlight is also of importance and free ventilation will encourage its entrance into wards Allied to free ventilation is proper bed spacing and distance between bed centres ideally not less than 12 feet and never less than 8 feet Patients suffering *from septic complications* should be be removed to cell or cubicle wards and if these are not available they should be nursed on the strictest bed isolation principles including face masking A high standard of aseptic nursing should be exacted and this takes for granted that adequate staff with

proper facilities for carrying out the technique is provided In many hospitals the transfer of patients to convalescent wards at a certain stage of illness will also be found practicable Such methods as the above have been carried out in many fever hospitals for a long period but in view of the high importance now attached to dust borne infection and the realisation that its dissemination is largely the result of disturbance of dust during bed making and sweeping has led to investigations which have as their object the suppression of dust Van der Ende and Thomas (1941) have devised methods of oiling bed clothes and floors which under experimental conditions would appear to go far in supplying a satisfactory solution to the problem Short of the adoption of oiling methods damp dusting and sweeping are imperative The prevention of aerial infection by droplet nuclei has been studied by Wells (1936) and the employment of ultra violet radiations and disinfectant mists and vapours may eventually do much to render safe the atmosphere of the large open ward Evidence of the success of dust suppression and aerial disinfection under routine conditions has been slow in accumulating and it is to this critical test that we must look for final proof of re infection as the cause of many of the complications of scarlet fever It cannot be denied that the doctrine is attractive and it has gained wide currency but some have been critical For example Scholes (1944) while not disputing the importance of cross infection does not regard it as an important cause of the serious complications of scarlet fever such as nephritis or primary scarlatinal rheumatism nor the preponderant factor in the minor ones Moreover when the policy advocated by Allison has been carried out in practice the results are not as favourable as might have been expected Bergmann (1944) reporting that of 100 scarlet fever patients treated in single bed wards 51 per cent escaped complications as compared with 32 per cent among an equal number accommodated in open wards It has never been asserted that re infection accounts for all the complications in scarlet fever and such opinions and findings do not make the pursuit of the highest standards of ward management any less desirable but they serve to emphasise the limitations of even the best systems of ward management

General Management Mild cases of the simplex type should remain in bed for ten to fourteen days but in the sharper cases the patient will not be able to get up in less than three weeks Complicated cases will require to remain in bed but when apyrexial and general conditions warrant it those with otorrhœa or rhinorrhœa take no harm from being up a little in the open air Diet during the febrile stage should be milk given in stated quantities at regular intervals with plenty of water imperial drink or still lemonade containing glucose between whiles When the temperature is normal milk puddings potatoes mashed with butter and other semi solids may be added for a day or two and thereafter the diet is augmented gradually with fish tripe or chicken until at the end of a fortnight the patient should be on a full mixed diet Blanket bathing should be carried out every day and when the patient is up daily hot baths may be given In the early stage the toilet of the mouth should be performed by swabbing the tongue gums and cheek with boroglycerine Local treatment of the throat is limited to frequent simple gargles but if faucial angina is marked gentle flushing from a douche can held about the level of the patient s head with hot soda bicarbonate solution (6 grs to 1 oz) every three hours is useful and comforting If the throat is painful enough to interfere with the proper nourishment of the patient ice cream will often be taken readily Should the temperature rise beyond 102 F tepid sponging will sometimes induce sleep In the early stages restlessness and mild delirium are usually controlled by aspirin but in more marked cases paraldehyde in 1 or 3 drachm doses will be required Aperients should be given if necessary and it is well to commence treatment with a brisk saline purge Routine daily testing of the urine should be carried out during the first four weeks of illness

Specific Treatment A considerable volume of recorded experience is now available on the treatment of scarlet fever by scarlet fever antitoxin and it is generally accepted that the serum exerts a specific action in the early eruptive stage of the disease Owing to the mild form of scarlet fever in Western Europe and America it has not been possible to apply the critical test of the effect of serum on fatality rates Also data concerning the effect on the toxic and septic types is

scanty but the general indications are that the results are encouraging especially in the toxic type as we might have expected from the early successes which were obtained by the use of convalescent serum For the most convincing proof of the specific action of the serum we rely on the clinical results in individual cases in the early eruptive stage of the disease and no one who has observed the results in even a small number of cases can fail to be impressed by the fact that these are well marked and constant The most striking effect is on the temperature and pulse which in the great majority of cases are brought to normal in twelve to twenty four hours The rash fades early and the patient experiences a rapid return to his usual well being This is contributed to by an abatement of the throat symptoms probably due chiefly to a reduction in faucial œdema as inspection of the throat shows little or no diminution of congestion or ulceration Subsequent desquamation may be scanty or when well marked may be slightly retarded in time of appearance or again in a proportion of cases it may

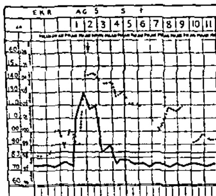


Fig 10 Temperature and pulse chart of serum treated case of scarlatina simplex Patient received 10 c c scarlet fever antitoxin (↓) Note rapid fall of temperature and less rapid fall of pulse rate



Fig 11 Temperature and pulse chart of serum treated case of scarlatina simplex Patient received 20 c c scarlet fever antitoxin (↓) Note rapid fall of temperature followed by rebound No complication was discovered to account for this

General Management Mild cases of the simplex type should remain in bed for ten to fourteen days but in the sharper cases the patient will not be able to get up in less than three weeks Complicated cases will *require to remain in bed but when* apyrexial and general conditions warrant it those with otorrhœa or rhinorrhœa take no harm from being up a little in the open air Diet during the febrile stage should be milk given in stated quantities at regular intervals with plenty of water imperial drink or still lemonade containing glucose between whiles When the temperature is normal milk puddings potatoes mashed with butter and other semi solids may be added for a day or two and thereafter the diet is augmented gradually with fish tripe or chicken until at the end of a fortnight the patient should be on a full mixed diet Blanket bathing should be carried out every day and when the patient is up daily hot baths may be given In the early stage the toilet of the mouth should be performed by swabbing the tongue gums and cheek with boroglycerine Local treatment of the throat is limited to frequent simple gargles but if faucial angina is marked gentle flushing from a douche can held about the level of the patient s head with hot soda bicarbonate solution (6 grs to 1 oz) every three hours is useful and *comforting* If the throat is *painful enough to interfere* with the proper nourishment of the patient ice cream will often be taken readily Should the temperature rise beyond 102 F tepid sponging will sometimes induce sleep In the early stages restlessness and mild delirium are usually controlled by aspirin but in more marked cases paraldehyde in 1 or 3 drachm doses will be required Aperients should be given if necessary and it is well to commence treatment with a brisk saline purge Routine daily testing of the urine should be carried out during the first four weeks of illness

Specific Treatment A considerable volume of recorded experience is now available on the treatment of scarlet fever by scarlet fever antitoxin and it is generally accepted that the serum *exerts a specific action in the early eruptive stage of* the disease Owing to the mild form of scarlet fever in Western Europe and America it has not been possible to apply the critical test of the effect of serum on fatality rates Also data concerning the effect on the toxic and septic types is

refined and concentrated serum should be injected intra muscularly into the lateral aspect of the thigh If a rapid drop in temperature and pul e do not appear within twenty four hours the dose should be repeated but if the expected result does not occur after one injection it will usually be found that the continued pyrexia is the result of early adenitis or otitis

In the toxic and septic types from 15 c c (15 000 U S A units) to 30 c c (30 000 U S A units) of the refined serum should be given intravenously and when this route is employed the various precautions enjoined in the section on serum reactions should be observed to prevent or minimise serum shock Serum sickness was expected to occur in from 20–30 per cent of all patients treated with the preparations of scarlet fever antitoxin in former use but with the refined product in our experience the occurrence of the condition has been exceptional

Chemotherapy The beneficial effect of the sulphonamide group of substances in experimental and natural streptococcal infections has led to their use in scarlet fever With a view to clearing up the early acute phase of the disease and the avoid ance of complications Hogarth (1937) has given sulphanilamide alone and in combination with scarlet fever antitoxin without significant effect Others however such as Peters and Havard (1937) have obtained a substantial reduction in complications with the same product Our own results obtained so far are in line with the former worker but further observations are necessary before definite conclusions can be reached In the treatment of already established complications conflicting results have also been obtained In some cases of adenitis quinsy otitis media and rhinorrhœa immediate and sometimes spectacular improvement has been obtained and cases of recovery in streptococcal meningitis following scarlatinal otitis are on record On the other hand the results of chemotherapy

doses Since the method of assay cannot be regarded as giving results of the d gree of accuracy poss ble in the titration of such substances as d pl theria and tetanus ant toxin official regulat ons providing for the standardisation of scarlet fever preparations have not so far been introduced in *the United Kingdom. The same att tude was adopted by the Health Organisat on of* the League of Nations which reported on this subject in 19 3 and 1931 For this reason we h ve g ven a olumetric dosage of scarl t fever antitox n as well as in U.S.A units

be suppressed Since scarlet fever now retains its importance largely on account of complications it is to the effect of serum in reducing these that we should look for convincing proof of its practical aid in treatment and most of those who have investigated this point have reported a diminution It should be noted however that the appearance of *complications in serum treated cases is by no means rare* and the administration of scarlet fever antitoxin cannot yet be regarded as presenting a complete solution to this most important problem This brief account of the results of serum treatment are those following on intramuscular injection but much more striking effects have been obtained by Banks (1933) who is a strong advocate of the intravenous route in practically all cases and by this method has reduced his complication rate to 4 2 per cent and the period of detention in hospital to between two and three weeks It is possible that the maximum therapeutic advantage of scarlet fever antitoxin can only be obtained from this method of injection but the ever present possibility of sharp immediate reactions has deterred many from following this practice as a routine in the ordinary case of scarlet fever in which at present the prognosis is excellent Subsequently Banks (1936) claimed equally good results from intraperitoneal injection which is free from the untoward reactions of the intravenous route By the majority of clinicians antitoxin is employed for all cases of the toxic or septic types and in the sharper cases of the simple type Accordingly in the latter group we are accustomed to give serum if the temperature is 102 F or above if the rash is very bright if there is well marked faucial angina if there is *delirium or much restlessness and in particular serum should* be given to all patients of five years or under unless the attack is of the mildest To be effective serum should be given as early as possible and in the simplex type doses of 3 c c (3 000 U S A units)[1] to 10 c c (10 000 U S A units) of the

[1] In the above observations on scarlet fever antitoxin the dose is given in both cubic centimetres and U S A units The latter are official in that country and have been promulgated by the National Institute of Health of the Federal Government which has established a standard serum as the fixed basis with which other scarlet fever antitoxins can be compared and a definite amount of this standard serum is defined as a unit This unit is 10 times the smallest amount of scarlet fever antitoxin necessary to neutralise one test dose of toxin each test dose representing 5 skin test

with fruit juice The bulk of cases will yield to this but in some in order to secure efficient action of the skin hot packs or the hot air bath will be required Again an alkaline mixture containing 30 grs each of soda bicarbonate and potassium citrate in an ounce of water three or four times daily may have a rapid effect *in clearing up the condition* If uræmia occurs 5–20 ozs of blood according to the age of the patient should be withdrawn and convulsions controlled by light anæsthesia The persistence of slight albuminuria in the late stages of the complications in spite of dietetic restrictions will sometimes yield to cautious additions of protein to the diet Finally when the kidney function has become normal the patient s anæmia will require treatment It has been suggested by Osman (1923) that large daily doses of alkali equal parts of soda bicarbonate and potassium citrate in 200 gr doses daily for those under seven years and 400 grs for those over that age is a valuable prophylactic against scarlatinal nephritis when given during the first three or four weeks of the disease

Adenitis may be treated simply by the application of cotton wool and a bandage but sulphanilamide and linseed poultices or cataplasma kaolin may hasten resolution in well marked cases If suppuration occurs hot boric fomentations should be applied and incision and drainage delayed until very obvious fluctuation is present

If *otitis media* gives warning of its presence by acute signs and symptoms penicillin treatment should be instituted at once and in a high proportion of cases the dosage outlined above continued for three or four days will usually produce rapid recovery The first sign however of acute otitis media in scarlet fever is usually otorrhœa and again penicillin should be given If this substance is not available treatment on conservative lines should be initiated by mopping out the ear thoroughly every three or four hours with a small pledget of wool securely attached to a wooden probe or forceps and finishing by mopping with methylated spirit or instilling a few drops of glycerine of carbolic When carried out conscientiously three or four times daily or more frequently when discharge is exceptionally profuse the bulk of cases will yield excellent results In a certain proportion of cases however these measures will fail and in order to prevent chronic ear

may sometimes be disappointing We are of the opinion however that unless there are indications to the contrary one of the sulphonamides should be prescribed either alone or in conjunction with penicillin if available particularly if the complication is severe At the outset the dosage should be high 3 9 gms per day according to age and diminished after two or three days

Penicillin The action of this substance in the treatment of scarlet fever has not yet been fully explored but so far as our preliminary observations go we have not been able to note any clinical effect on the eruptive stage In the treatment of a limited number of pyogenic complications it has been effective particularly in otitis media in which the results have been very promising and it certainly should be employed in all cases of the septic type of the disease and in all severe complications due to streptococcal invasion At present until its therapeutic efficiency is defined it might be as well to combine its administration with one of the sulphonamides A total daily dosage of 240 000 units should be given by the continuous intramuscular drip or 30 000 units given by intramuscular injection every three hours

Treatment of Complications Early *arthritis* is treated by rest of the affected joints radiant heat from the electric cradle if the pain is severe and the local application of oil of winter green The later arthritis of the rheumatic type associated with endocarditis is treated on the same principles as acute rheumatism and prolonged rest will be required In a few cases of this type we have seen striking benefit result from the intravenous injection of scarlet fever antitoxin in 10 or 20 c c doses in the early stages but whether this result was attributable to a specific or a non specific action must be left open Pericarditis should be treated by the administration of penicillin and sulphonamides and drainage of the pericardium may be necessary Suppurative arthritis will require the assistance of the orthopædic surgeon

In *nephritis* the patient is put in a blanket bed and the skin encouraged to act with hot bottles A saline purgative *e g* sulphate of soda is given and the patient put on a milk diet until the urine is clear for a few days Abundant glucose should be supplied preferably in the form of drinks flavoured

acute toxæmias intravenous injection of 5 per cent glucose in saline by the continuous drip is indicated Extreme delirium occasionally encountered in these cases will need full doses of morphine and hyoscine

Septic scarlet fever apart from serum penicillin and sulphonmides does best on an open air regime and the patient s strength supported by liberal and frequent feeding and abundance of fluids one or other of the proprietary foods such as Bengers and solutions of glucose being most suitable Difficulties are almost certain to arise however in the true septic case as nourishment is resisted on account of pain and difficulty in swallowing In these cases the nasal tube may be employed with advantage and we have occasionally tempted small children to swallow appreciable quantities of ice cream In those who will tolerate it gentle douching of the throat with hot soda bicarbonate solution every two hours should be carried out and judicious swabbing with glycerine of carbolic will be helpful Local treatment however will nearly always be strenuously objected to and the consequent exhaustion may cancel any probable benefit The various complications such as suppurative adenitis otitis media and mastoiditis bronchopneumonia and empyema and suppurative arthritis should be dealt with on the lines already indicated

Period of Isolation It is now the practice in the majority of fever hospitals to release scarlet fever convalescents not suffering from complications at the end of four weeks and in actual practice we have found it possible to discharge slightly over 30 per cent of our scarlet fever patients at this time whilst by the end of seven weeks between 70 and 80 per cent of our patients have returned home It is possible that the period of four weeks may be still further reduced and in this country and America periods of three and even two weeks have been tried without deleterious results Gordon (1934) who has made an extensive study of this aspect of scarlet fever in Detroit declares that we have been too much guided in the past by routine measures applied to patients in the mass and that it would be much more scientific to deal with each case on its merits He points out that infectivity persists chiefly in the winter months and in young children and varies his isolation period accordingly between four three and even two

discharge it may be necessary to recommend removal of tonsils and adenoids as the first step to bringing about a healthy naso pharynx When this is established the aural condition may subside but if there is no indication for this operation or if it fails then to obtain permanent cure a mastoid operation will require to be undertaken Should signs of *acute mastoiditis* be present in addition to acute otitis media when the patient comes under observation penicillin combined with sulphon amide administration should be commenced pending the decision of the otologist as to the necessity for operation In *streptococcal meningitis* treatment by penicillin and sulphon amides holds out the best prospect of success

Rhinorrhœa is often an intractable complication and is an indication for plenty of fresh air Gentle nasal douching with sodium bicarbonate biborate and chlorate 2 drachms of each to the pint should be carried out three times a day if the patient is old enough to co operate Insufflations of dimol snuff applied twice daily by means of an atomizer are also useful while some prefer nasal instillations of argyrol drops As an adjuvant to these procedures the nasal mucosa may be sprayed beforehand with adrenalin The nostrils should be smeared with zinc ointment to prevent excoriation and in small children constant swabbing is necessary to prevent dis charge infecting the conjunctivæ In chronic cases the services of the rhinologist should be sought for the correction of defor mities in the nose or for the treatment of pathological conditions in the para nasal sinuses

Broncho pneumonia requires abundant fresh air frequent nourishing feeds and oxygen should be given early by means of an oxygen tent or by the nasal catheter Linseed poultices should be applied to the chest and at the first sign of the complication treatment by penicillin and sulphathiazole should be begun Careful watch should be kept for a streptococcal pleural effusion and if this occurs, repeated aspiration should be performed and pencillin introduced into the pleural cavity Later if the effusion becomes purulent surgical drainage will be necessary

Toxic Scarlet Fever In addition to the specific treatment outlined above the patient requires frequent hot packs and hypodermic injection of strychnine or coramine As in most

another person opportunities for direct contact *e g* kissing should be avoided and they should have their own towels crockery and cutlery set apart School or work should not be resumed for a fortnight after release from hospital and patients should be in the open air as much as possible

weeks As we have seen Banks has reduced his period to under three weeks by intravenous injection of serum and Benson in Edinburgh has discharged patients at the end of three weeks who had no serum treatment When these minimal periods of hospital isolation are adopted it is a wise precaution to arrange for an examination of the patient and urine a week or two subsequent to discharge Such periods apply only to clean cases those showing catarrhal or suppurative discharges requiring isolation until these have ceased A certain proportion which become chronic and resist all the resources of hospital treatment are usually permitted to return home at the end of twelve weeks but such cases should not be lost sight of and should be referred for further medical supervision

Return cases of scarlet fever are defined as those arising in individuals who have been in contact *e g* at home or in an institution with a person whose isolation for scarlet fever has recently been terminated They are usually recorded as a percentage of the total annual scarlet fever admissions but it is now also customary to state the infecting case rate as well *i e* the percentage of cases responsible for return cases calculated on the total annual number of scarlet fever patients discharged from hospital From the earliest days of isolation hospitals much thought has been expended on their prevention but in spite of the most elaborate precautions these unfortunate occurrences cannot be eliminated and such infecting case rates as 2 or 3 per cent seem inevitable in the present state of our knowledge Patients should be examined with meticulous care before discharge to make sure that they are free from all clinical signs of infection and in some hospitals the system of discharge blocks or convalescent wards is in vogue Convalescents are sent to these for varying periods before going home to remove them from the more infectious environment of acute scarlet fever wards The occurrence of common colds immediately after discharge is undoubtedly responsible for lighting up infectivity and the patient should be warned to avoid these as far as possible Probably the most important precautions are those advised to be taken by the patients themselves for a week or two after their return home They should not sleep in the same bed or the same room if possible as

prevalence from the last few to the first few months of the year has taken place during the last fifty years He has also found that in London and Glasgow incidence is highly correlated with overcrowding Whilst the disease may occur at any age its main incidence is upon infants in the first few months of life and in adults between forty five and fifty five males suffering more frequently than females In common with other infectious diseases erysipelas has declined as a factor in mortality from 95 per million in 1871–80 to 21 per million in 1921–30 Mortality is very high in the new born and during the first few months of life diminishes greatly in the ten to twenty age period whilst thereafter it steadily increases with age The case fatality for all notified cases varies a good deal from year to year Hospital rates are usually higher since such cases are subject to a process of selection on the grounds of severity or poor social circumstances and for the ten year period ending 1937 in the Edinburgh City Hospital have fluctuated between 3 9 and 14 2 per cent with an average case fatality of 8 3 per cent in 1 700 cases In the past the attention of many has been attracted by the apparent close association in seasonal incidence between erysipelas puerperal sepsis and scarlet fever but modern statistical workers incline to the belief that there is no real correlation one with the others

Transmission Whilst outbreaks of erysipelas were common in the pre antiseptic era these are now unusual and we can only recollect one or two instances in our own experience when case to case infection was a possibility In searching for a source of infection in erysipelas investigation must not be limited to the attempt to find an associated case of erysipelas since an individual suffering from almost any form of streptococcal sepsis or a nasopharyngeal carrier of streptococcus pyogenes may be the source There is also some reason to believe that occasionally infection may be autogenous in that the occurrence of a common cold may produce a sudden increase in the number of pathogenic streptococci in the nasopharynx and an infecting dose of these may be carried to a nidus suitable for the inception of the characteristic lesion We have noted that a substantial number of cases of erysipelas are preceded by what the patient describes as a cold and Anderson (1939)

CHAPTER II

ERYSIPELAS

Synonym—The Rose St Anthony s Fire

Pathology The observation by Fehleisen in 1884 that the disease is caused by a streptococcus has been amply con firmed and whilst bacteriological works state that the organism can be most readily isolated from the spreading margin of the lesion we have never found difficulty in obtaining hæmolytic streptococci in pure culture from the fluid in blebs by plating directly on to blood agar Several have claimed that hæmo lytic streptococci from erysipelas form a well defined group but studies of their serological characteristics and toxigenic properties have failed so far to provide convincing evidence of any group specific relationship to the disease In common with other strains of streptococcus pyogenes they fall into Lancefield s group A and one or other of Griffith s serological types Whilst erysipelas may occur in mucous membranes for example in the fauces or larynx its characteristic site is in the skin usually or the face The organisms multiply in the lymphatic spaces of the cutis and produce a spreading inflammatory œdema Occasionally localised abscesses occur or extension into the subcutaneous tissues may produce a cellulitis The marked constitutional disturbances associated with sharp cases of the disease must be attributed to un differentiated toxins liberated by the organisms at the site of proliferation No specific immune substances have been satisfactorily demonstrated so far in the blood of erysipelas patients or in experimental animals Apart from œdema of the skin at the site of the erysipelatous process post mortem changes are limited to those of an acute toxemia or to those denoting such complications as broncho pneumonia Occasion ally pyemic abscesses yielding streptococci are found

Etiology Erysipelas has a world wide distribution and in the United Kingdom shows a well marked seasonal incidence the period of highest prevalence being from December to May According to Russell (1933) this movement of the maximum

some part of the skin surface and on examination the typical features of erysipelas present themselves In the great majority of cases these will be found on the face commencing at the inner angle of the eye on the bridge of the nose at the nostrils or on or near the ear The process however may originate on any part of the body starting from an obvious wound in the new born from the umbilical stump or in less obvious sites on the scalp or limbs particularly the legs The lesion shows at first as an irregular patch of dusky erythema of uniform intensity This is tender painful and shiny with a well defined raised edge which in the course of a few hours will be found to have spread Œdema is also characteristic and in facial erysipelas the face generally is swollen whilst if the process involves the eyelids these are puffy and closed Similarly if the skin of the ears is invaded these are greatly thickened and painful As the inflammation extends over the skin blebs containing amber fluid form on parts already involved and if the spread continues these may scab and dry up the skin originally involved losing its angry appearance and becoming the seat of a brown scaly desquamation With the widening of the area of spread the rate of progress tends to slow down and extension occurs by the fitful appearance of patches of the characteristic erythema Usually after two or three days to a week the condition fades out When erysipelas commences on the face in the neighbourhood of the eye or nose it quickly spreads to both cheeks giving a butterfly pattern and it may spread to the ears or up over the brow to the scalp the sub cutaneous tissues of which become œdematous Extension to the body from the face is not very usual but this may occur by way of the scalp and the back of the neck setting up wandering erysipelas in which the inflammation may spread over nearly the whole of the skin surface Such severe infec tions are relatively rare In erysipelas neonatorum the process quickly spreads from the umbilical stump to the abdomen genitals and buttocks and is sometimes almost fulminating in character with extensive formation of bullæ and sloughing of skin Erysipelas has been held to commence in the larynx giving rise to acute œdema of the glottis and it is occasionally noted in the fauces which become greatly œdematous plum coloured and sloughy In cases of puerperal sepsis we have

reports the observation that the onset of many cases of facial erysipelas is preceded by a tonsillitis pharyngitis and rhinitis Transmission in the past has been regarded as almost entirely manual and this will readily occur by means of contaminated hands and instruments unless complete asepsis is maintained in performing surgical procedures but the fact that the *role* of the nasopharyngeal carrier of pathogenic streptococci is now widely appreciated means that droplet infection may also be a mode of spread The portal of entrance is through a breach in the skin or mucous membranes and whilst this may be obvious as for example when erysipelas occurs in a surgical wound on the other hand it may be microscopic

Infectivity If strict asepsis is carried out the infectivity of erysipelas is negligible and cases can be readily nursed in open wards with other patients on bed isolation principles

Incubation Period This is short and usually given as from 2 to 8 days The imposition of quarantine on contacts is unnecessary

Clinical Features Erysipelas has been classified into various types such as *traumatic* when the skin lesion commences at a wound or *idiopathic* when it appears without any obvious breach in the skin or mucous surface The assumption in the past that in the idiopathic case the breach is microscopic is regarded as unnecessary by Anderson (1939) who suggests the use of this term for cases preceded by an early acute inflammation of the upper respiratory tract Again clinicians often classify the disease into *facial* and *corporeal or wandering* according to the part or parts affected while the term *phlegmonous* erysipelas has been applied to cases showing subjacent extension to the cellular tissues In all however the skin lesion and the constitutional disturbances are essentially the same

The period of invasion is usually short and the appearance of the rash is not long anticipated by the abrupt onset of the constitutional disturbances usually associated with an acute febrile illness Thus there are rigors vomiting various degrees of headache and a steep rise of temperature to 102 or 104 F The patient is obviously ill at ease restless and may quickly become confused and delirious The site of the *local lesion* is disclosed by pain often described as burning or stiffness on

monest complication in facial erysipelas *Acute nephritis* is not an unusual complication whilst in severe cases *hypostatic pneumonia* and *broncho-pneumonia* are frequently seen Whilst not strictly speaking a complication delirium tremens is apt to appear during the course of erysipelas in alcoholics

Relapse and Subsequent Attack *Relapse* is a relatively common event in convalescence from erysipelas and occurs in approximately 5 per cent of cases Whilst a relapse is generally less severe than the primary attack especially in respect of constitutional disturbance this is not invariable and we have

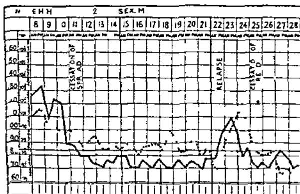


FIG 13 Temperature and pulse chart of primary attack with relapse of facial erysipelas Patient was treated with sulph anilamide for first ten days after admiss on and for four days after onset of relapse

seen one and even two relapses in the same patient of greater severity than the original illness *Second attacks* are also relatively common and Ker states that no fewer than 17 per cent of his erysipelas patients gave a previous history of having suffered from the disease on one or more occasions As an extreme instance of this tendency to recurrence we may say we have had under observation a patient who suffered from no fewer than ten severe attacks over a period of three years

Diagnosis The characteristic inflammation of the skin and the well marked constitutional reaction usually make diagnosis fairly evident Various patchy erythemata such as *serum rashes* localised to the site of injection may give a fair imitation of the rash of erysipelas but the absence of pain constitutional

observed a similar condition in the vaginal mucosa accompanied by much superficial necrosis the subsequent spread to the vulva and surrounding skin leaving no doubt as to the true nature of the lesion The lymph glands in anatomical relationship to the site of the lesion are usually swollen and tender

Although in some instances *constitutional disturbances* in erysipelas are minimal as a rule they are sufficiently well marked to render the disease one of some severity The patient is restless and often confused while in some especially alcholics, the excitement may be almost maniacal The mouth and tongue are dirty the patient is usually constipated although diarrhœa may be present in some cases Albuminuria is common The pulse is rapid and of poor volume whilst quickened respirations when the disease has been present for a few days may denote hypostatic or broncho pneumonia With the onset the temperature rises quickly to 102 or 104 F and may be continuous in type should the condition only remain active for a few days resolution being by crisis or a quick lysis In a fair number of cases however it may be swinging in character especially if the process be prolonged In the latter case toxemia may be profound exhaustion extreme and from the restless delirium of the early stages the patient may pass into coma death occurring from heart failure Occasionally the temperature shows unmistakable signs of resolution with a definite improvement in the general condition before the spread of skin inflammation has wholly come to an end Attacks of the disease even when relatively short leave the patient in an enfeebled condition and convalescence is slow

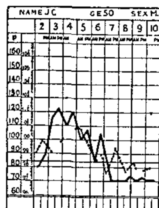


FIG 12 Temperature and pulse chart of case of facial erysipelas Spread ceased on sixth day

Complications *Localised abscesses* especially in the scalp and *cellulitis* are relatively common and in our own experience various degrees of *sloughing of the eyelids* are by far the com

was undertaken must obviously be factors of importance Whilst we must assume that with sulphanilamide at our disposal in treatment cases of wandering erysipelas must become less frequent a glance at the temperature chart here reproduced must convince anyone that this form of the disease is bound to produce severe exhaustion and that in view of the possible occurrence of heart failure or pneumonia a guarded prognosis should be given Occurring as an intercurrent disease in scarlet fever since this usually occurs in persons at favourable age periods we have usually found the disease relatively mild but in puerperal sepsis the occurrence of erysipelas especially of the prolonged type must add to the gravity of the outlook Alcoholics do badly as do those the victims of privation and uncertain mode of life Marked delirium broncho pneumonia and coma are all of very serious import Occasionally anxiety may arise as to local end results when extensive sloughing of the eyelids has taken place Our experience has been that a considerably greater amount of repair is obtained than has been anticipated when the sloughing is at its worst

Prophylaxis Erysipelas retains its place in the list of notifiable diseases largely because those responsible for the administrative measures necessary for prevention of infectious disease are desirous of having information of the occurrence of streptococcal disease generally Accommodation is provided by the majority of local authorities in their isolation hospitals with a view to securing the necessary medical and nursing attention which the disease in many cases undoubtedly requires Institutional outbreaks are now practically unknown but such cases as occasionally occur should be promptly isolated and in addition a careful investigation should be made of all those in association with the patient so that latent streptococcal infection in a contact may be disclosed Active immunisation of those subject to the disease has been attempted by means of streptococcal vaccines and the injection of toxins derived from streptococci isolated in erysipelatous lesions but with unproved success In those subject to recurrent attacks of facial erysipelas it may be well worth undertaking a thorough examination of the nasopharynx and the paranasal sinuses since chronic inflammatory foci may provide a

disturbance and bullæ would be against that disease It must be admitted however that in mild cases of true erysipelas the formation of bullæ *may not occur* but the scaly *desquamation* following the subsidence of erysipelas is usually present *Erythema nodosum* is often confused with erysipelas but the usual appearance of the former on the shins and the multiple lesions fading into the surrounding skin should enable a distinction to be made *Cellulitis* is also often reported as erysipelas and the dividing line between the two conditions must often be slender especially in those forms of localised cellulitis which occur in the course of generalised streptococcal

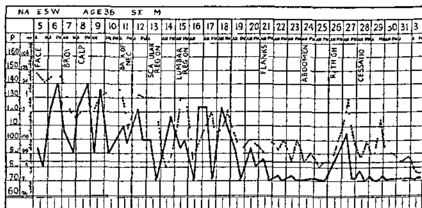


FIG 14 Temperature and pulse chart of wandering erysipelas The case was untreated by sulphonamide and began with the usual butterfly pattern on the face

infections *Dermatitis* in the neighbourhood of chronic varicose ulcers is also sometimes confused with erysipelas but again it is by no means an uncommon occurrence for the latter disease to originate in such lesions The absence of a febrile reaction with constitutional disturbance and the raised spreading edge of erysipelas would decide in favour of a simple dermatitis

Prognosis As has been noted the disease is most fatal in the very young or the aged whilst females have a better chance of survival than males at all ages In individual cases a guarded prognosis should be given in those subject to chronic disease especially of the kidneys whilst in those in whom erysipelas has supervened in operation wounds the condition of the patient prior to operation and the condition for which operation

recommended by Ude and Platou (1930) two or three exposures of about one and a half or twice the erythema dose being administered over the spreading edge of the lesion by means of a mercury vapour lamp

Chemotherapy Of recent years the methods mentioned above have been largely discarded in favour of treatment by the sulphonamide group of drugs which have been regarded by many as almost specific in their action on erysipelas In much of the published work however the total therapeutic advantage to be derived from these substances is obscured by the fact that the number of cases has not been large that the cases so treated have been controlled by cases unrelated to the epidemic in which treated cases have occurred or by cases treated by methods such as phototherapy for which beneficial results have already been claimed The series reported by Snodgrass and Anderson (1937) falls into the last category but their conclusions would probably be accepted by all who have frequent opportunities of studying the effect of sulphanilamide They found that this substance was of benefit in securing curtailment of the duration of spread of the skin lesion the duration of primary pyrexia and the duration of toxemia whilst complications and the tendency to recurrence were reduced In a more recent communication Anderson (1939) claims that adequate chemo therapy cures erysipelas in practically all cases within three or four days and to secure this result recommends sulphanilamide in a daily total dosage of 5–9 gms for adults 4 o–6 gms for children aged five to ten years and 3 gms for those under five years The drug should be given four hourly by the mouth and full dosage employed until the temperature returns to normal Thereafter 0 5–1 grm should be given for ten to fourteen days When this is done recurrence is said to be unusual Our own personal investigations into the effects of sulphanilamide lead us to the same general conclusions and there can be little doubt that the administration of this drug on the lines suggested is a definite advance in the treatment of erysipelas

Penicillin This remedy has also shown itself to be of considerable value in the treatment of erysipelas So far our experience of its use has been limited mainly to severe cases in aged patients but practically all have responded well The

reservoir of infection from which repeated attacks may be derived

Treatment The patient should be isolated with all aseptic precautions throughout the illness Good nursing is essential and the patient should be given as liberal a diet as can be contrived in the shape of frequent small feeds of milk glucose any of the proprietary foods jellies chickentea porridge cream, pounded fish chicken and eggs In the stage of exhaustion occurring in the course of a prolonged illness intravenous glucose by the drip method is necessary Another most important point in treatment always emphasised by Ker was the necessity for securing sleep for the patient at the outset of the illness We have usually found 10 grs each of aspirin and veronal sufficient for this but when delirium is present a full dose of morphine is often required If the pulse is unsatisfactory hypodermic injections of strychnine or coramine should be given whilst intercurrent pneumonia requires treatment on the usual lines With regard to the local treatment of the skin lesion innumerable preparations have been recommended but we know of none that is likely to promote the arrest of the erysipelatous process The most that can be hoped for is amelioration of pain and the diminution of the intensity of the inflammation and for this no local application is better than a saturated watery solution of magnesium sulphate to which as Benson (1930) recommends 10 per cent of glycerine may be added With the introduction of the sulphanilamide preparations however magnesium sulphate is contra indicated and we have found a local application of equal parts of Lassar s paste and ichthyol very useful A satisfactory method of treatment by specific immunisation has long been sought Thus scarlet fever antitoxin has been widely employed in erysipelas whilst serum prepared on the same lines from strains of streptococci derived from erysipelas have also been tried In our experience neither of these has produced any demonstrable effect on the disease and Benson (1930) who has made a careful study of treatment by vaccines has come to a similar conclusion in respect of this mode of specific treatment Until the introduction of recent chemo therapeutic methods perhaps the most encouraging results in treatment of erysipelas have been secured by phototherapy as

CHAPTER III

PUERPERAL SEPSIS

Nomenclature The occurrence of sepsis in the genital tract following labour has been variously termed Childbed Fever Milk Fever or Puerperal Fever Since however the infection may be related etiologically to one or other of a number of organisms and result in a variety of clinical manifestations it *is better to use the comprehensive* designation of Puerperal Sepsis

Pathology The commonest causal organism in puerperal sepsis is streptococcus pyogenes which in our experience at the North Western Hospital occurred in about 45 per cent of all forms of the condition Practically all strains fall into Lancefeld s Group A and one or other of Griffith s serological types B coli accounted for about 22 per cent whilst the remainder were ascribed chiefly to non hæmolytic streptococci anaerobic streptococci staphylococcus pneumococcus gono coccus and B Welchii On gaining access to the genital tract a local sepsis is set up in the endometrium by one or other of these organisms and in a certain proportion of cases this is favoured by such concomitant conditions as trauma or retained placenta In the great majority of cases the sepsis remains localised the febrile reaction being the result of local inflam mation and toxæmia Inflammation may spread however and this is particularly the case when streptococcus pyogenes is the invader Should there be infected lacerations of the cervix and vagina extension may occur by the lymphatics to the tissues at the base of the broad ligaments giving rise to pelvic cellulitis and possibly pelvic abscess Or again spread may take place to the peritoneum According to Fry (1934) this results most commonly from a septic thrombo phlebitis of the small veins of the uterine wall and to a much less extent from spread by the Fallopian tubes If the inflammation remains localised to the pelvis there ensues a pelvic peritonitis characterised by matting of the pelvic organs and loops of bowel or abscess formation usually in the pouch of Douglas Extension however may involve the abdominal peritoneum

effect on temperature is not immediate this seldom falling to normal until treatment has been continued for three or four days but spread of the inflammation is arrested early the inflamed area loses its angry appearance œdema is rapidly reduced and the patient s return to comparative alertness is quickly brought about The last mentioned is due to the disappearance of toxic symptoms in one or two days a striking feature and while it is impossible as yet to draw comparisons with sulphonamides in the treatment of erysipelas or to give indications for the use of one substance in preference to the other we think that the advantages obtained in the rapid reduction of toxæmia are worthy of being weighed against the admitted disadvantages of the three hourly or four hourly injections These results have been obtained by the administration of a total daily dosage of 120 000 to 240 000 units

above mentioned Committee (1930) stating that death was due to this cause in 53 per cent of all maternal deaths in primiparæ Whilst half the deaths from sepsis reviewed by this Committee occurred after spontaneous delivery in the other half difficult labour with trauma was an antecedent factor As a result of the latter finding the Committee were of the opinion that among predisposing causes the most important were injury to tissues exhaustion and hæmorrhage With regard to environment as long as a definite source of infection could be excluded unhygienic and crowded dwellings and dirty surroundings did not in themselves increase the incidence of sepsis With the introduction of modern obstetric methods the outbreaks of puerperal sepsis which were a feature of lying in hospitals in the past have now largely disappeared the majority of deaths from sepsis occurring in single and sporadic cases

Transmission A potential source of infection is the vulva and the skin of the perineum of the patient from which staphylococci colon bacilli bowel streptococci and B Welchii may be carried on the hands and instruments of the attendant into the genital tract if obstetric technique is defective Of recent years considerable attention has been directed to the method of transmission of infections due to streptococcus pyogenes It has been established that the organism is practically never present in the birth canal before labour and the observations of Smith (1927) and D C Colebrook (1935) point practically conclusively to the source of infection being an attendant or contact of the patient or the patient herself One or other of these may be suffering from a latent or patent oral or naso pharyngeal infection the droplet spray disseminated during talking etc gaining direct access to the birth canal or being carried thence on hands or instruments at or within a day or two of delivery Finally the source of infection in institutional outbreaks may be another patient suffering from puerperal or other form of sepsis the infecting organisms being spread by manual transmission by contaminated articles such as instruments or bed pans or dust

Incubation Period The first sign of puerperal sepsis commonly occurs within 3 or 4 days after labour Signs however may be delayed for 7 or 10 days and even up to 3 weeks

with consequent general peritonitis associated occasionally with a generalised blood infection Again a septic thrombo phlebitis may be set up in the uterine veins and spreading to the iliac veins give rise to femoral thrombosis Septic emboli may become detached and produce a wide range of apparent localisation in various structures suppurative arthritis, cellulitis of the subcutaneous tissues broncho pneumonia and pulmonary abscess empyema endocarditis and pericarditis being probably the commonest Invasion of the blood stream directly from the uterus may result in general septicæmia and while there may be an obvious septic process in the uterus to account for this on occasion the naked eye appearances at post mortem amount to very little It should be understood that while the main paths of the spread of inflammation have been traced in this brief account any combination of these may be found Post mortem findings present therefore a wide diversity of lesions

Etiology Puerperal sepsis was reported on as the chief main cause of maternal mortality in the series of deaths reviewed in the Final Report of the Ministry of Health Departmental Committee on Maternal Mortality and Morbidity (1932) this cause accounting for 37 per cent of all maternal deaths In 1934 the puerperal sepsis mortality as recorded by the Registrar General was 1 59 per 1 000 live and still births in England and Wales and while there was reason to believe it had remained fairly constant for a good many years it is now diminishing the corresponding figure for 1940 being 0 54 The same satisfactory decline has occurred in Scotland where the puerperal sepsis rate is estimated as per 1 000 live births From 3 13 in 1934 it declined to 1 54 in 1940 While some diminution in the sepsis mortality may be ascribed to the introduction of the regulations widening the definition of puerperal fever to include puerperal pyrexia in 1926 those with any clinical experience of the condition must attribute the diminution mainly to the development of the sulphonamide drugs which began about 1936 Case fatality rates in our large fever hospitals at present are approximately 5 per cent but it should be borne in mind that an increasing proportion of these is due to post abortive sepsis Primiparæ are more vulnerable to sepsis than others the Interim Report of the

either singly or in combination such cases account for about 10 per cent of all cases of puerperal sepsis Also in our experience about 60 per cent of all such cases are the result of infection by streptococcus pyogenes In addition to the signs of local uterine sepsis constitutional disturbance is well marked The patient is flushed anxious and sleepless Pain sometimes intermittent in the lower abdomen is complained of and may be acute Abdominal tenderness with some degree of rigidity is elicited on palpation and a palpable mass may be defined in one or both iliac fossæ Examination per vaginam may reveal tenderness or thickening in the fornices or the characteristic induration of pelvic cellulitis After several weeks of exhausting fever with swinging irregular temperature resolution of the inflammatory products occurs the temperature gradually settles and the patient improves Or again improvement sets in with the pointing of an abscess in the region of the inguinal ligament per vaginam or per rectum

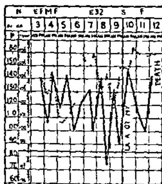


Fig 1[illegible] Temperature and pulse chart of fatal case of puerperal general peritonitis due to streptococcus pyogenes Patient did not receive sulphonamide and a laparotomy was performed

General Peritonitis This is caused by streptococcus pyogenes in about 75 per cent of such cases in our experience *B coli* accounting for the majority of the remainder whilst staphylococcus pneumococcus and non hæmolytic streptococcus are also occasionally found The condition usually appears in the first three or four days of the puerperium especially in the most severe and rapidly fatal cases but in a minority it may be delayed till the second or rarely the third week The signs of local sepsis are well marked as a rule They are accompanied by a sharp rise in temperature and rigors while from the first the patient looks ill with anxious expression and slightly drooping eyelids Rigors may be repeated and the temperature fluctuates irregularly between 100 and 104 F with a bounding pulse of 120 to 160 Abdo

Clinical Features The onset of signs of puerperal sepsis is usually fairly sudden and the patient complains of chills whilst actual rigors are not uncommon The temperature rises quickly and may be anything from 101° to 105° F the pulse is rapid and rates of 130 to 160 are often found Headache nausea restlessness and insomnia are often present but pain is unusual at most the complaint being of lower abdominal discomfort On examination there may be tenderness over the lower abdomen and the uterus bulky and sub involuted *Lochia* may be scanty brownish in colour and of a foul odour

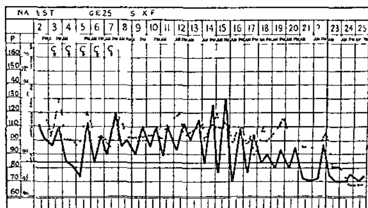


Fig 15 Temperature and pulse chart of case of pelvic cellulitis due to B coli infection Patient treated with intra uterine glycerine (ç) and sulphanilamide

or abundant and frankly purulent A few cases may present an apparently normal lochia whilst on the other hand there may be entire suppression On examination of the birth canal there may be all degrees of damage to the perineum vagina and cervix lacerations being sloughy and if repair has been carried out after labour the tissues are œdematous with the stitches cutting through In about four fifths of cases of puerperal sepsis the infection remains at the stage of *local uterine sepsis* and with appropriate treatment the temperature and pulse rate subside in from a day or two to a week convalescence being quickly established

Pelvic Cellulitis and Peritonitis Extension of the inflammatory process may give rise to pelvic cellulitis or peritonitis In actual practice some degree of both is often present and

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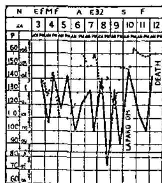


Fig 16 Temperature and pulse chart of fatal case of puerperal general peritonitis due to streptococcus pyogenes Patient did not receive sulphonamide and a laparotomy was performed

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minal signs and symptoms at first may be inconclusive general peritonitis taking twenty four to forty eight hours to declare itself In early cases palpable swellings with tenderness and some rigidity in the lower abdomen can be made out sometimes but pain is variable and at first generally absent abdominal discomfort being the main complaint *Distension and diarrhœa* are the most important early signs of general peritonitis At first the abdomen remains soft Later extreme distension may result in drum like tightness but the board like rigidity associated with peritonitis following rupture of a viscus is absent Later also free fluid may be demonstrated and vomiting hiccough and pain added to the miseries of the patient She retains consciousness almost to the end which comes in from a day or two to a week and is heralded by clamminess a straight line temperature chart and flagging pulse

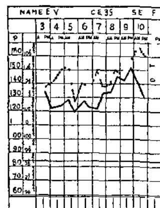


FIG 1 Temperature and pulse chart of puerperal general septicæmia due to streptococcus pyogenes The *steady level of pyrexia* from the second to the seventh day of illness was exactly similar on the four hourly chart Note also rapid pulse rate

General Septicæmia In our experience this is due to infection by streptococcus pyogenes in about 70 per cent of cases B coli *staphylococcus pneumococcus* non hæmolytic streptococcus and anaerobic streptococcus being found in the remainder The intervening period between labour and the onset of fever may be from a few hours up till the usual three or four days It is marked by a quick rise of temperature to 102 or 104 F with rigors rapid pulse possibly hurried respirations and restlessness Signs of local sepsis may or may not be well marked but from the onset the patient looks seriously ill sallow and dehydrated Rigors are repeated and the temperature follows a steady course at the level to which it originally rose the four hourly chart even showing remarkably little deviation The pulse is rapid from 130 to 160 and blood culture discloses the nature of the condition If the patient survives long enough signs of broncho pneumonia with pleural

effusion or empyema acute arthritis of shoulder elbow hip or knee endocarditis or pericarditis and various intensely painful dusky erythematous patches in the skin of upper arms or forearms point to cellulitis In the majority of cases the patient lapses into the typhoid state low muttering delirium merging into coma and death in the course of seven or 10 days In those that recover the blood becomes sterile but extensive and severe localisation of the infection in one or other of the sites mentioned leads to a prolonged and stormy convalescence

Thrombo phlebitis In the somewhat restricted sense in

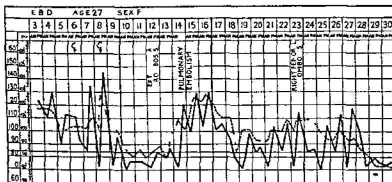


FIG 18 Temperature and pulse chart of local uterine s psis followed by left femoral thrombosis and pulmonary embolism later by r ght femoral thrombosis Patient was a multipara and abundant streptococcus pyogenes was recovered from the cervix Int a uterine glycerine was g ven (ʢ)

which this event can be recognised clinically as a manifestation of puerperal sepsis its commonest occurrence is in the femoral vein and for the condition Wyatt (1938) suggests the term puerperal femoral thrombosis It appears most commonly between the tenth to thirtieth day of the puerperium and is preceded by a local uterine sepsis which may have spread to the pelvic cellular tissue or peritoneum The onset is accompanied by a recurrence or recrudescence of pyrexia and well marked constitutional disturbance with shivering and malaise Pain in the groin knee calf or ankle of one limb is complained of and tenderness may be made out along the line of the femoral vein Swelling may begin in the foot or thigh but in the course of a day or two the whole limb is involved After

several days the pain and febrile reaction subside but the swelling may take anything from four to eight weeks or longer to resolve and in a few cases some residual swelling may be permanent In from a few days to a fortnight from the onset in one limb the same sequence of events may occur in the other in about half the cases Even with the most careful management these cases in our experience are prone to be complicated by pleurisy and pulmonary embolism and occasionally by cerebral embolism Recovery is the rule except when the condition forms part of a severe and protracted general infection

Complications and Association with other Diseases Apart from localisation of infection from the primary focus in various organs or tissues certain other morbid conditions are found relatively often in association with puerperal sepsis Of these the commonest are the *urinary infections* which in our experience may be expected in about 20 per cent of cases The frequency of B coli as the causal organism is high about 80 per cent a small proportion being due to streptococcus pyogenes These infections may be symptomless and are only discovered during the routine bacteriological examination of the urine but on the other hand they may be accompanied by a high temperature and rigors In spite of a marked febrile reaction the patient s well being is fairly well maintained appetite and sleep being relatively good Occasionally however pain and tenderness in the loins frequency of micturition and dysuria are complained of The condition in the past has often proved intractable and even when the acute febrile stage has been passed the persistence of organisms in the urine indicates a lingering infection *Mastitis* is found as a concurrent complication in about 10 per cent of cases of puerperal sepsis whilst *puerperal insanity* in which the patient is highly excitable and difficult to control or in a state of acute depression is occasionally met with The variant of *surgical scarlet fever* sometimes produced by the implantation of streptococcus pyogenes in the genital tract at labour and the intercurrence of *erysipelas* in puerperal sepsis have been mentioned in the sections on scarlet fever and erysipelas respectively

Diagnosis The onset of fever after labour or miscarriage

should always be taken to indicate puerperal sepsis until the contrary is proved The signs of local uterine sepsis will usually be fairly obvious but a complete examination including a bi manual should be carried out since the main problems in diagnosis arise in the attempt to assess the amount of spread of infection Bacteriological examination is essential also A swab from the vagina is considered by some bacteriologists to be all that is necessary but in hospital practice the patient is usually put up in the lithotomy position and a swab taken from the cervix brought into view by means of a speculum The diagnosis of septicæmia depends on blood culture which should always be carried out in patients with pinched worn out expression high temperature tachycardia and repeated rigors In the case of general peritonitis it should be remembered that the cardinal signs of this condition are abdominal distension and diarrhœa Owing to the relative frequency with which urinary infections occur as complications of puerperal sepsis catheter specimens should be obtained for prompt transmission to the bacteriologist and several examinations may be necessary before the cause of a puzzling pyrexia can be brought to light

Prognosis In puerperal sepsis prognosis depends to a considerable extent on the nature of the infecting organism In approximately 70 per cent of puerperal sepsis deaths the causal agent is streptococcus pyogenes and moreover in the graver forms of the condition such as pelvic peritonitis and cellulitis general peritonitis and septicæmia the probability that this will be the infecting organism is high In local uterine sepsis the prognosis is good and the patient s recovery is complete in two or three weeks The risks of a fatal termination in pelvic peritonitis and cellulitis are also not great but the patient may undergo an illness of six to ten weeks before convalescence is established Cases in which femoral thrombosis supervenes will also suffer a long illness recovery from time to time being delayed by pulmonary complications Death in puerperal sepsis is almost entirely the result of generalised spread to the peritoneal cavity or the blood stream In the pre chemotherapeutic era the prognosis in puerperal peritonitis was very grave and while a few ca es recovered the most favourable survival rate in any series of cases was unlikely

method of atmospheric sterilisation with the aerosol devised by Pulvertaft and others (1939) will be necessary to overcome this In the meantime every care should be taken to secure adequate ventilation and thorough cleanliness of lying in wards and rooms

Since the introduction of sulphonamides the question has arisen as to the practicability of employing these in the prophylaxis of puerperal sepsis but Colebrook and Kenny (1936) have drawn attention to the undesirability of indiscriminate administration of these drugs apart from special circumstances Such special risks might arise when there was a possibility of infection by hæmolytic streptococci and Hoare (1939) in this event suggests the administration of 1 grm daily of sulphanilamide or sulphapyridine beginning as soon as labour starts and continuing for three or four days While recognising that toxic effects are sometimes produced by these drugs we believe Hoare s suggestion has much to commend it and the practice might well be extended to any case in which trauma has occurred during labour or in which sepsis might be anticipated

Treatment In treatment good nursing with scrupulous attention to aseptic methods is absolutely essential and with the decline in typhoid admissions the puerperal cases have largely come to take their place as providing the supreme test of the skill watchfulness and devotion of the fever nurse Although we must confess to meeting with a certain amount of difficulty in persuading our puerperal patients to accept it abundant fresh air and open air treatment if possible is of considerable service in improving their general condition The patient should be supported in bed by pillows in the Fowler position to encourage drainage from the uterus and assiduous nursing care is necessary to promote complete mental and physical rest It is important to realise that almost the first requirement of many puerperal sepsis patients is sleep and aspirin veronal or paraldehyde will usually be effective Special attention may also be necessary to remove sources of discomfort by the use of the breast pump the relieving of an over full bladder or taking out stitches which are beginning to cut through œdematous and inflamed perineal tissues If it is considered practicable to keep the baby on the breast and quite a number of mothers with minor degrees of sepsis

will be able to continue feeding their infants this should be persevered with but except at feeding times the mother should not be distracted by its presence When the infant is not being breast fed a daily visit is usually enough to satisfy the mother as to the baby s condition In the febrile stage diet will be milk chiefly but this can be varied with tea coffee or cocoa and suitable proprietary foods and the patient should be encouraged to drink large quantities of fluid in the form of plain water glucose in fruit juice or barley water In the great preponderance of cases management on the above lines combined with the local treatment described hereafter will be all that is necessary and provided the temperature and pulse have been settled for about a week the patient will be allowed up By this time she will have been taking a full mixed diet and convalescence is quickly established Since anæmia is present in a high proportion of patients iron preparations are frequently required at this stage

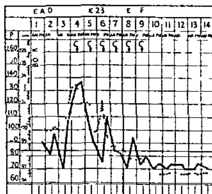


Fig 19 Temperature and pulse chart of case of local uterine sepsis in a multipara Streptococcus pyogenes was recovered in pure culture from the cervix and the condition rapidly cleared up after repeated daily injections of intra uterine glycerine (Ç)

Local Treatment This should be initiated as soon as possible after the patient comes under observation and our routine practice is to combine it with the careful local examination which is carried out in the lithotomy position With the usual precautions a catheter specimen of urine is first taken The vaginal speculum is then inserted and after careful inspection of the parts a swab from the cervix is taken for bacteriological examination Opportunity is then taken to give *intra-uterine glycerine* This results in immediate benefit to many cases the temperature falling to normal in the next twenty four to forty eight hours with an abatement of all signs and symptoms

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prostration paræsthesia headache visual disturbances or joint pains Apart from the effect produced on established infections several have expressed the opinion that as a result of chemotherapy the spread of the pathological process is arrested so that infection is limited to the site of implantation and does not progress to the severe generalised blood and peritoneal forms The case then for the administration of sulphanilamide or sulphathiazole is exceptionally strong and at the first sign of rigor pyrexia or other initial sign the patient should be put on one or other of these drugs forthwith in 6–12 grm doses daily according to circumstances the daily amount being halved after the first two days or otherwise reduced and the drug discontinued after eight or ten days from the commencement

Penicillin Therapy No wide experience can yet be claimed in the use of penicillin for the treatment of puerperal sepsis but in patients suffering from severe forms of infection due to penicillin sensitive organisms such as streptococcal or staphylococcal septicæmia or peritonitis and in widespread pelvic peritonitis and cellulitis we have obtained results superior to those following the use of any other method including chemotherapy The clinical picture in patients suitable for treatment shows remarkable improvement in a few days Administration of the substance should be begun immediately on the identification of a penicillin sensitive organism as the cause of infection 100 000 to 200 000 Oxford units being introduced daily through the medium of a continuous intravenous drip of glucose saline for at least five days In certain patients improvement may only be temporary and one or even more courses of penicillin may be required while such complications as pelvic abscess or pyosalpinx may require surgical treatment

Accessory Methods of Treatment Special developments or complications of puerperal sepsis may call for efforts in addition to the outlines given above For example in *general peritonitis* if paralytic ileus supervenes suction of the bowel contents by the intestinal tube must be combined with the penicillin and glucose saline drip In *pelvic inflammations* lower abdominal pain requires the application of heat by means of fomentations or poultices and in these conditions we have obtained valuable assistance from the electric cradle

a soft rubber catheter into the cervix as far as it will go without pressure and holding it in place by means of forceps A record syringe containing 20 cc warmed glycerine is then attached to the catheter and the contents gently expressed into the uterus Much of it leaks back but enough is retained to promote free drainage from the uterine wall and in addition pieces of retained placenta and clot may be expelled Some leave the catheter *in situ* retained by a suture or a self retaining catheter is employed so that the treatment may be repeated every few hours Others add iodoform or other disinfectant to the glycerine but we have found that daily injections repeated until the discharge has ceased to be purulent give all the benefits to be expected from this method Obviously if there is abdominal pain or a tendency to hæmorrhage intra uterine glycerine is contra indicated Otherwise local treatment consists in douching with Liquor Sodæ Chlorinatæ or other antiseptic lotion When fragments of retained placenta are present or in post abortive cases when membranes have not been expelled the uterus is gently cleared out with the gloved finger under general anæsthesia

Chemotherapy Until the introduction of the sulphonamide compounds it was difficult to be enthusiastic about any line of treatment in the major degrees of puerperal sepsis Chiefly used in the past were immuno transfusion intravenous serum of various types including scarlet fever antitoxin in large amounts injection of mercury and organic arsenic compounds and the administration of vitamin concentrates In our hands we cannot say that any of these special methods justified themselves Such results however as those reported by Foulis and Barr (1937) and Colebrook and Purdie (1937) have induced a much more hopeful outlook particularly in strepto coccal septicæmia and general peritonitis The striking results achieved by the former pair of workers were obtained by the injection of soluble prontosil or the oral administration of prontosil album in daily amounts of from 3 to 14 grms Red prontosil soluble prontosil and sulphanilamide were all employed by Colebrook and Purdie who express a slight pre ference for the two former They recommend an initial daily dose of 8–15 grms in the very severe cases the quantity to be reduced on the appearance of such toxic effects as cyanosis

CHAPTER IV

DIPHTHERIA

Synonym—Membranous Croup for the laryngeal form of the disease

Pathology The disease is caused by the Corynebacterium diphtheriæ which almost invariably gains a lodgment in the mucous membranes of the upper respiratory tract but may do so also in other mucous membranes and through abrasions of the skin Locally the organism produces a specific inflammatory reaction which is shown by the formation of pseudo membrane whilst a powerful exotoxin diffuses into the circulation and causes the general toxæmia characteristic of the disease This as far as clinical observation is concerned is manifested by disturbances in the circulatory nervous and renal tissues but it is doubtful if any system escapes with the possible exception of the brain Post mortem examination of fatal cases apart from the presence of membrane reveals toxic changes chiefly in the heart kidney and liver these being represented histologically by fatty degeneration and necrosis in the parenchyma and in the case of the two former by interstitial changes as well Naked eye lesions *e g* hæmorrhages are not uncommonly found in the adrenals and on histological examination marked degenerative changes will usually be found in cases fatal in the early stages of the disease Although morphological and serological differences have long been recognised in members of the group defined as true diphtheria bacilli it was believed that these had little bearing on the pathogenesis of the disease Anderson and McLeod and their co workers (1933) have however classified various types of diphtheria bacilli by cultural and biochemical reactions and these types have been correlated with the clinical severity of cases of diphtheria They have been named *gravis intermedius* and *mitis* types the two former being associated with the severe and fatal forms and the last with milder infections A considerable volume of work has given results in general agreement with these findings After a post mortem study of

When beginning this treatment exposure should only be for a few minutes at a time and the temperature should not go above 105° F since the effect on some patients is very depressing Later temperatures of 110 to 115° F can be borne for half an hour In *femoral thrombosis* compresses of lead and opium may be applied to relieve pain and the affected limb or limbs swathed in cotton wool and immobilised between sand bags measures also being taken to prevent drop foot Elevation of the foot of the bed for 6 or even 12 inches hastens resolution of the swelling while massage is indicated in the later stages In *broncho pneumonia* chemotherapy will almost certainly be already employed and this may be supplemented by poulticing stimulation by strychnine or coramine and oxygen therapy Pleural effusion must be watched for and treated by repeated aspiration while later operative measures to drain the pleural cavity may be needed The services of the orthopædic surgeon should be sought at an early stage for the treatment of arthritis In the *urinary infections* which so frequently accompany puerperal sepsis 40 gr doses of equal parts of sodium bicarbonate and potassium citrate every four hours will usually clear up the subacute afebrile forms of the condition In the presence of an acute febrile reaction however sulphanilamide in 1 5–3 0 grms daily will be necessary to render the urine sterile

and immune reactors show no trace of reaction at either test or control sites of injection When the individual tested is sensitive to the non specific protein constituents of the reagent *pseudo reactions* appear and these require careful scrutiny when the final reading of the test is made In persons immune to diphtheria but sensitive to the proteins in the reagent a small area of erythema will occur in about twenty four hours at the site of both test and control injections but will usually disappear by the fourth day after injection and will not go through the characteristic stages of pigmentation and desquamation although small indefinite stains may remain for about a week Such combinations of reactions are termed *combined pseudo negative* Persons susceptible to diphtheria and sensitive to the proteins in the reagent will also give erythematous reactions at the site of both test and control injections but in these the reaction at the test area tends to be larger and passes definitely through the stages of pigmentation and desquamation whereas the erythema at the control area disappears early Such reactors are termed *combined pseudo positive* Pseudo reactors are generally found among adults and adolescents and in those who have previously had injections of horse serum or diphtheria prophylactics In doubtful cases when a reading is difficult it is wise to regard the individuals concerned as positive and susceptible The optimum times to make readings of the Schick test are the fourth and tenth days but if only one reading can be made and this is usually the case when work on a large scale is being carried out an interval of one week between the performance and scrutiny of the test fulfils all practical requirements The main factor influencing immunity to diphtheria is age and the following table sets out the results of Schick testing scarlet fever and measles patients of both sexes at the North Western Hospital London

The percentage susceptibility rate at all ages shown on p 70 is practically identical with that of 61 2 found in Edinburgh by Ker (1924) who has compared his figure with that of Zingher (1917) in New York scarlet fever patients viz 45 per cent It will be ob erved that the highest susceptibility rates are grouped round the age periods between one and four years and thereafter immunity increases with age although the downward trend of the curve is uneven in the fifteen to thirty

fatal cases of diphtheria McLeod and others (1939) have reported that gravis infections produce a severe and generalised toxic effect on the viscera associated with haemorrhagic necrosis of the tonsils penetrating to the deeper tissues and involving the cervical lymph nodes whereas in mitis cases obstruction in the respiratory passages from membrane formation is the usual cause of death Intermedius infections give a picture nearer to gravis than mitis

The Schick Test This immunity reaction is carried out in the human subject for the purpose of estimating individual immunity to diphtheria and is performed by the intradermal injection of a test dose of standardised diphtheria toxin adjusted so as to be contained in 0 2 c c volume this being controlled by the injection of a similar amount of toxin inactivated by heating Originally the Schick test dose was presumed to distinguish those with $\frac{1}{30}$ of a unit or more of circulating toxin per cc of the blood from those with less but apparently there is no absolute relationship between antitoxin titre and reaction to the Schick test dose Those with as much as $\frac{1}{30}$ of a unit will certainly be Schick negative but several workers including Leach and Poch (1935) have demonstrated that many persons with as little as $\frac{1}{100}$ of a unit and even less may be Schick negative Nevertheless we agree with the preponderance of those who have had any considerable practical experience of the test that a negative Schick reactor will have in nearly all cases a complete immunity to diphtheria whilst in the remaining few the immunity is sufficient to limit the disease to a modified and benign form The test and control are generally performed on the flexor surfaces of the left and right forearms respectively A *positive and susceptible reactor* shows a patch of erythema at the site of injection in from twenty four hours to five days and in the great majority of cases this will be well defined at the end of forty eight hours It reaches a diameter of from 10 to over 30 mm and the erythema is most pronounced at the seventh to tenth day thereafter fading but showing well marked brownish staining and desquamation Pigmentation may not disappear for about a month and in pronounced cases for two or three months In very highly susceptible patients vesiculation may occur within a few days of the injection *Negative*

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Table showing Schick positive percentages in 2 905 Scarlet Fever and Measles Patients

Age in years	Total	Schick negative	Schick positive	Per Cent positive
0–½	18	16	2	11 1
½–1	78	29	49	62 8
1–2	304	74	230	75 7
2–3	323	71	252	78 0
3–4	297	64	233	78 4
4–5	287	92	195	67 9
5–10	933	387	546	58 5
10–15	286	169	117	40 9
15–20	129	67	62	48 1
20–30	158	90	68	43 0
30–40	62	43	19	30 6
40+	30	21	9	30 0
Total	2 905	1 123	1 782	61 3

age period the result probably of one or other of the factors which are known to influence natural immunity to diphtheria Dudley (1934) believes this is brought about by repeated exposure to subclinical doses of C diphtheriæ i e doses insufficient to cause recognisable diphtheria but sufficient to stimulate the production of specific antibodies It follows therefore that in crowded urban populations among which the diphtheria bacillus is always present the general level of immunity will be higher than in rural communities where human contacts are less frequent and intensive For similar reasons social status is an important factor in determining immunity to diphtheria children from well to do homes showing a higher susceptibility rate than their contemporaries in less fortunate circumstances Schick testing in populations subject to such geographical and social factors has given results in general agreement with what we should expect on the above hypothesis of the development of natural immunity

Etiology *Diphtheria appears in epidemic form chiefly in* the cold and temperate zones during the winter months in Great Britain the highest incidence occurring between December

and March Originally a rural disease the diphtheria mortality in the county boroughs of England is now twice that of the rural districts according to Greenwood (1935) Relatively rare under one year of age the disease is commonest between one and ten years reaching its maximum between the fourth and sixth years and gradually falling off in adult life The sex incidence is about equal up till the ninth year after which females are attacked more often Diphtheria is now the principal cause of death during school life and the Registrar General for England and Wales (1934) has pointed out that since the beginning of this century there has been a progressive change in the incidence of diphtheria mortality from the pre school to the school age As far as can be determined this is not due to a shift in the age incidence which remains the same at these age periods but according to H D Wright (1939) is the result of a proportionately smaller decline of the fatality rate in the 5–9 than in the 0–4 age period Picken (1937) suggests that this may be due possibly to a change in strain of C diphtheriæ while Cheeseman Martin and Russell (1939) are inclined to attribute the alteration mainly to diminution in the average size of the family and to a less extent to improving environment In common with a number of other infectious diseases diphtheria in modern times has shown a waning severity and a League of Nations Epidemiological Report (1934) has pointed out that if the death rate of children under 15 in England and Wales be taken as 100 for the quinquennium 1856–60 and compared with the rates for the quinquennium 1926–30 the fall in the diphtheria death rate is 78 per cent Due allowance must be made for the introduction of diphtheria antitoxin in 1895 but Woods (1933) states that about 1880 the mortality began to decline Following the widespread immunisation campaign carried out in the United Kingdom during the war years 1941–45 the fall in diphtheria mortality has been accentuated For some years before the 1939–45 war hospital case fatality rates were generally about 5 per cent but there is some evidence that the immunisation campaign has also affected these the figure given for Scotland for example in 1944 being 2 6 per cent Case fatality rates in diphtheria however must be accepted with caution as so much depends on the stringency with which diagnosis is

carried out Possibly one factor which operated to reduce diphtheria mortality rates in the inter war period was the diminution in incidence of the laryngeal form of the disease

Transmission The source of infection may be a case of the disease or a carrier and the organism is disseminated by droplet infection although more obviously direct methods of contact such as kissing or the common use of drinking vessels must often be responsible Epidemics have occurred in which milk was the vehicle of infection but outbreaks of this character have not been common in this country of late The milk may be contaminated by droplet infection from a carrier but Savage (1937) mentions a few milk outbreaks in which diphtheritic ulceration of the udder was present While the organism is capable of retaining its viability apart from the human host for varying periods under suitable conditions fomites cannot altogether be excluded but in modern public health practice little importance is attached to these Defective drains are not now regarded as a direct cause of diphtheria and the consensus of veterinary opinion is against the probability of transmission by domestic animals The causal organism usually gains admission to the body by inhalation but infection of wounds abrasions of the skin or extra respiratory mucous surfaces occasionally occurs

Infectivity When estimated by the occurrence of clinical diphtheria in contacts the disease is one of moderate infectivity and in hospital wards spread may be prevented by the bed isolation nursing An infected person is capable of transmitting the disease as long as the organism remains viable in the tissues and in diphtheria patients bacteriological examination indicates that it usually disappears in three or four weeks from the onset in the great majority of cases In a certain proportion however particularly those with pathological or anatomical abnormalities in the naso pharynx the organism persists for a considerable time after clinical recovery such *individuals being classified as convalescent carriers*

Incubation and Quarantine Period The incubation period is short usually one to four days the maximum limit being six or seven days Quarantine periods are rarely observed in contacts isolation being continued only until their freedom from infection is established by obtaining two or three consecu

tive negative swabs together with frequent clinical examination of nose and throat whilst awaiting bacteriological results

Clinical Features Diphtheria is typically an infection of the *upper respiratory tract* and the most common sites of the local manifestations are the fauces the nasopharynx the larynx and the anterior nares *Non respiratory* infections of the skin wounds genitals and conjunctivæ may also occur but in all situations the pathological reaction is essentially the same Accordingly for purposes of description diphtheria is usually classified on an anatomical basis and this method has been accepted by a committee consisting of members of the infectious hospital service of the London County Council in a report on the Nomenclature of Diphtheritic Infections (1936) In the account of the various types which follows the terms recommended in that report have been adopted in their entirety As will be seen anatomical classification has a significance beyond mere description for according to site one or other of the clinical features of the disease may predominate and consequently influence treatment and prognosis It should be clearly understood also that one of the outstanding characteristics of the local lesion in diphtheria is its tendency to spread and therefore one or more of the above anatomical sites may be progressively involved For example it is not uncommon for faucial diphtheria which fails to receive specific treatment at an early stage to spread to the nasopharynx and the larynx

Faucial Diphtheria This is termed tonsillar diphtheria by some and may be defined as occurring when membrane is limited to the tonsillar surfaces with possibly slight spread to the anterior pillars of the fauces The stage of invasion is short and usually accompanied by fever headache general malaise and nausea Some degree of sore throat is complained of but this may not be a prominent symptom even when pseudo membrane is already present The latter commences as a thin gelatinous exudate on one or both tonsils usually continuous but occasionally beginning to form at several points simultaneously so that a follicular appearance is presented If wiped off the exudate rapidly re forms and in a short time thickens up giving the typical appearance of diphtheria membrane dead white or greyish yellow in colour

with a well defined margin By this time it can only be detached with difficulty leaving a raw bleeding surface *Apart from some congestion near the edge of the membrane* the fauces show little deviation from normal unless there is a super added septic infection There may be more or less oedema of the tonsils but pain is not severe even on swallowing It is also doubtful if the characteristic odour of diphtheria will be very obvious in the type here described Associated with the throat condition there will be slight or moderate enlargement of the tonsillar glands The initial pyrexia of 100–103° F

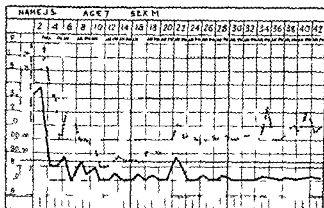


FIG 20 Temperature and pulse chart of first six weeks of recovered case of severe nasopharyngeal diphtheria Patient received 50 000 units of antitoxin intravenously (↓) Note apyrexial course of temperature and rapid drop of pulse rate up till tenth day

rapidly subsides when the patient is brought under treatment but *there is no characteristic temperature curve and in this* as in all types of diphtheria the patient may be apyrexial from the start The pulse is rapid and soft at first but slows down in a few days A little pallor and limpness may be noted the urine in this type is usually free from albumen and *with appropriate treatment the throat quickly clears up* The toxaemia *varies from slight to moderate in amount* and the ordinary case of faucal diphtheria runs an uneventful course except for the occasional appearance of one or other of the common pareses in convalescence

Anterior Nasal Diphtheria *When limited to the anterior* nares diphtheria is a relatively harmless infection as far as the



FIG 21 Bullnecking and toxic appearance of severe case of nasopharyngeal diphtheria



FIG 2 Diphtheritic infection of chickenpox lesion The base of the necrotic ulcer is formed by the pectoral muscle Note discoloration of skin round ulcer

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patient himself is concerned the chief danger being in the readiness with which transmission to others may be effected The main clinical feature is the presence of a persistent thin watery and often blood stained nasal discharge The nostrils are encrusted and raw the upper lip swollen and excoriated and the face spotty Careful examination of the nares will sometimes reveal membrane Since toxæmia is absent or minimal there is little or no constitutional disturbance and the condition readily yields to specific treatment without complications

Nasopharyngeal Diphtheria This condition usually commences as a faucial infection and owing to the almost complete absence of natural immunity or delay in seeking specific treatment spread of membrane rapidly takes place from the tonsils to the faucial pillars the uvula soft palate the pharynx, the post nasal mucosa with its extensions and the anterior nares so that membrane can occasionally be seen protruding from the nose In early cases the membrane may be gelatinous but since usually these cases have reached an advanced stage before coming under the eye of the practitioner it is dirty yellow or blackened Faucial œdema is marked but that part of the palate uncovered by membrane retains its normal appearance A profuse continuous sero sanguineous discharge pours from the no e and cervical adenitis with periadenitis is a conspicuous feature so much so that the term bull necking is aptly applied The typical odour of diphtheria is very apparent and the patient shows a marked pallor not infrequently waxy and cyanotic in character He lies limp drowsy and apathetic breathing noisily with open mouth through the accumulation of membrane and secretion at the back of his throat Although lethargic he retains consciousness and in certain cases there is marked irritability restlessness and delirium The temperature possibly raised at first as in less severe infections falls in twenty four or forty-eight hours and the pulse is rapid and of poor volume The output of urine may be reduced to a few ounces per day and may even be suppressed Marked albuminuria is found and occasionally blood and casts as well With energetic specific treatment some degree of amelioration can be brought about in the local lesions and the toxæmia but in many cases this is only temporary and early clinical

manifestations of the effect of the toxin on the circulatory system become evident during the second week of the disease in the signs of heart failure which frequently proceeds in a few days to a fatal termination Should this be surmounted the patient still has dangers to face in the shape of one or other of the severe paralytic sequelæ or a late heart failure *Post nasal diphtheria* is a term sometimes applied to this form of the disease in young children As was pointed out by Marfan (1905) direct infection of the adenoid pad may be the primary lesion in these subjects and the extent of visible membrane may be an unreliable guide to the severity of infection as on ordinary inspection of the throat some of the gravest cases may show relatively small amounts of membrane limited to the inner surface of the tonsils Profuse nasal discharge faucial œdema periadenitis prostration and pallor give the clue to the gravity of the situation Harries (1933) indicates a further danger in this type of infection in that direct spread from the nasopharynx to the lung may produce a diphtheritic broncho pneumonia

Laryngeal Diphtheria Most commonly the larynx is invaded secondarily from the nasopharynx and primary laryngeal diphtheria must be regarded as rare The condition is serious on account of the resulting obstruction to respiration This is due to the presence of membrane and œdema of the larynx whilst the element of spasm and the accumulation of secretions in the trachea and main bronchi seems also to play a part Toxæmia is not a prominent feature unless faucial or naso pharyngeal lesions are well marked in which case the patient undergoes the same risks as when these forms alone are present The signs and symptoms are those of acute laryngitis followed by respiratory obstruction if the process is not arrested and it is customary to describe three stages according to the degree of involvement The *initial* stage is marked by hoarseness quickened respiration frequent and characteristic brassy cough and some degree of pyrexia If the condition progresses the *spasmodic* stage is reached This is shown by aphonia stridor on both inspiration and expiration and spasms of dyspnœa During these the face is flushed and cyanosed the eyes prominent and suffused and the terrified patient tosses about his bed in a vain effort to gain a more favourable

respiratory posture The soft parts of the lower intercostal spaces the epigastrium and at the root of the neck are seen to be sucked in on inspiration At first the spasms do not last for long and intervals of less laboured breathing occur in which some rest may be obtained but eventually the spasms become prolonged recession becomes exaggerated and the stage of *permanent obstruction* is reached The condition is now desperate respiration becomes shallow and sighing exhaustion is complete the pulse is fluttering and the patient livid Unless operation brings relief death occurs from asphyxia Occasionally advanced cases are seen in which laryngeal implication is part of a general respiratory involvement including all parts of the bronchial tree Again ca es are met with in which the diphtheritic process mainly affects the trachea and bronchi with the result that there may be little interference with the voice and the characteristic cough is lacking Nevertheless signs of recession and oxygen lack are well marked and this type is usually fatal

Aural Diphtheria True diphtheritic infections of the middle ear occur by way of extension from the nasopharynx but this form of diphtheria is much less common than is generally supposed Apart from bacteriological examinations it is difficult to understand how a diagnosis of this condition can be made It cannot be too strongly emphasised that a diagnosis based on the morphological features of a diphtheria like organism should never be accepted as establishing the presence of aural diphtheria which can only be proved by biochemical and virulence tests and by the estimation of the immunity of the individual

Extra respiratory Diphtheria In the great preponderance of cases diphtheria will be found in one or other of the above mentioned situations but it is well to remember that diph theritic lesions may occur elsewhere especially in children infection being conveyed from the nose or throat to wounds or abrasions Such may be found on the vulva prepuce and anus whilst circumcision wounds are sometimes infected Accidental wounds and sores of all kinds including chickenpox lesions may also be secondarily infected Whilst it is true that membrane formation takes place the accessibility of these lesions to surgical dressings may tend to prevent the recognition

of typical membrane The presence therefore of a progressive pathological process unyielding to the usual applications and associated with tissue destruction blackening and undermining of the skin should lead to the suspicion of diphtheria and thorough bacteriological examination Diphtheritic conjunctivitis is not uncommon and here typical membrane and œdema is more likely to be recognised Skin diphtheria gives rise to an impetiginous lesion with much crusting and if the process is unchecked localised gangrenous areas may form

Toxæmia of Diphtheria Whilst it cannot be doubted that diphtheria toxin exercises a powerful effect on nearly every tissue of the body the fact remains that after the early phase when the throat has cleared up the main clinical evidence of toxæmia is to be found in disorders of the cardio vascular and nervous systems and it is to the recognition and treatment of these that the efforts of the physician will be chiefly directed

Cardio vascular System in Diphtheria Owing to the marked reduction in the proportion of deaths in diphtheria from the laryngeal form of the disease heart failure is now responsible for the majority of diphtheria deaths and in many cases which recover various circulatory disturbances occur which may give occasion for anxiety Since the disease was first established as a clinical entity by Bretonneau the heart has been the subject of much investigation but it cannot be said that the position is other than obscure Some such as Warthin (1924) and Marvin (1925) would be inclined to attribute heart failure in diphtheria to myocardial degeneration Others such as Gunson (1917) have pointed to failure in the peripheral circulation as being an important additional factor while Harding (1920) concluded that essentially there is an oligæmia *chiefly quantitative in the early stages and qualitative in the later* Electrocardiographic studies apart from demonstrating all grades of myocardial degeneration have not thrown much light on pathogenesis so far although Alstead (1932) is inclined to postulate the existence of a factor additional to the gross changes in the myocardium revealed by the electrocardiograph Friedemann and Elkeles (1934) as a result of clinical histological and electrocardiographic studies believe that the pathological changes in the vascular system have become the central problem in diphtheria, and that heart failure is due

to a certain extent at least to lesions in the coronary vessels Those with an extensive experience of diphtheritic heart failure will be inclined to agree that while clinically attention is apt to be focussed on the gross changes in cardiac rhythm and impulse there seems little doubt that the peripheral circulation is also implicated

Signs of cardiac failure occur relatively early in the disease from the beginning of the second week onwards Patients in whom it occurs are commonly those who have suffered a severe attack of nasopharyngeal diphtheria in which the pulse rapid and of small volume at first gradually slows down towards the end of the first week Some degree of improvement may have been shown in response to serum treatment but the patient is still pale and inert albuminuria may have persisted and early palatal paresis is often present While in the average case heart complications develop over several days the onset may be sudden with profound collapse Generally however this stage is postponed for several days during which the blood pressure gradually falls off the first sound is softened to be followed by muffling of both sounds and the apex beat moves out to the nipple line Cardiac arrhythmia appears in the shape of extra systoles reduplicated second sounds or missed beats and becomes progressively more marked until the rhythm is completely disorganised In spite of this the patient may remain symptomless inert and continue to take nourishment and at any stage the heart signs may begin to clear up We have observed on rare occasions cases which even pursued a favourable course after a gallop rhythm had been established In most cases however well marked arrhythmia is followed by signs of collapse vomiting of bile stained fluid fainting

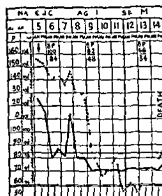


Fig 23 Temperature and pulse chart of fatal case of severe nasopharyngeal diphtheria Note steep fall in pulse rate and blood pressure Patient received 100 000 units of antitoxin (↓)

attacks in which the patient is almost pulseless and pre cordial pain Consciousness is retained but the patient is

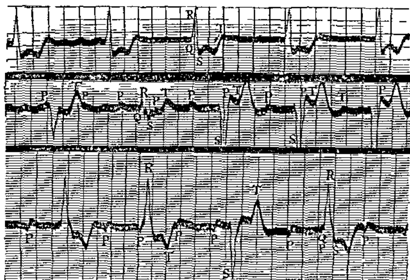


Fig ~4 Electrocardiogram showing complete heart block with bundle branch block Taken on seventh day of a severe and ultimately fatal case of nasopharyngeal diphtheria

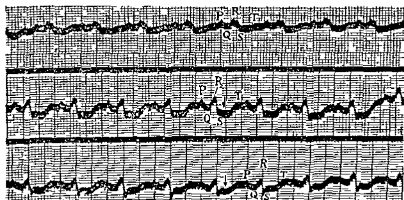


Fig ϑ Electrocardiogram showing delay in intraventricular conduction Taken on fourteenth day of diphtheria in a ase with advanced myocarditis which proved fatal on the eigthteenth day

apprehensive and whilst usually inert may become extremely restless By this time the apex beat is displaced well outwards and the area of liver dullness increa ed Electrocardiographic

records show various types of heart block This state may be drawn out for several days the patient shows a ghastly pallor wastes rapidly, nothing can be retained by the mouth attacks of retching and vomiting are frequent and death comes usually *in a fainting attack* *A later variety of heart failure in the third or fourth week* or after is much less common It generally appears in cases which have been severe from the first or have come late under specific treatment and may display all grades of severity from a symptomless arrhythmia to cardiac failure and in fatal cases heart block is frequently found Occasionally also circulatory failure may be coincident with or follow pharyngeal or respiratory paralyses and this would appear to be of a central origin In addition to the above forms immediate heart failure following sudden effort may occur in those who have shown relatively little in the shape of cardiac involvement and the strictest precautions must be taken in the management of the diphtheria convalescent to avoid this When recovery from heart failure in diphtheria takes place it is usually complete Irregularities may persist for some months and cardiologists have reported lesions met with in later life which can be traced to diphtheria but considering the great amount of degenerative change which is inevitable in the cardio vascular tissues of many the reparative process must be regarded as remarkable

Post diphtheritic Paresis and Paralysis There is no unanimity regarding the pathogenesis of these relatively common sequelæ of diphtheria The conception which has dominated neurological opinion in Great Britain is that of Walshe (1918) who believes that the complete symptom complex consists of three elements The first is an initial local paresis related anatomically to the site of the infective focus which is brought about by the passage of toxin along the perineural lymph channels to the nuclei of the cranial or spinal nerves The lesion is thus central and not merely an ascending neuritis in the afferent nerves The second element is selective in that diphtheria toxin has a special affinity for certain nuclei *e g* that controlling the nerve supply to the ciliary muscle whilst the third element polyneuritis may be regarded as the expression of the general toxæmia as it affects the nervous system and both these latter mentioned *elements are probably pro*

duced by toxin circulating in the blood stream Some fever clinicians however have been reluctant to accept this view For example Ronaldson (1935) is inclined to agree with some of the French writers that paresis results from a selective affinity of the toxin carried in the blood stream for certain nerve structures and points to the sequelæ of several accidents with diphtheria prophylactics which have provided examples of an artificial but true diphtheritic toxæmia in the human subject These were followed by *nervous sequelæ very similar* to those resulting from natural nasopharyngeal diphtheria and while believing that a strictly local action at the site of infection accounts for precocious palatal paresis Ronaldson takes the view that regional tissue diffusion of the toxin is the most likely explanation of paresis in the neighbourhood of the infective focus Mitman (1935) has put forward the interesting theory that paresis depends on the transportation of toxin from the site of infection along nerves to cranial nuclei those nearest the site of entry being the earliest most frequently and severely affected The toxin then travels from one nucleus to another within the central system the common sequence of paralysis being thus explained Whatever hypothesis is invoked to account for the paretic phenomena it should be noted that function is completely lost in a small minority of cases that the various palsies succeed each other in a fairly definite order after the lapse of a relatively constant latent period between the onset of disease and the appearance of the particular paralysis that recovery is the rule that pain and tenderness are only likely to occur in polyneuritic lesions in very severe or untreated cases and that disturbances of sensation are not likely to be encountered except in the most severe forms of generalised paralysis They occur in about 10 per cent of cases are commonest in children and are seen chiefly after severe cases or those coming late under treatment The following are characteristic and may occur singly or in combination

Palatal paralysis is the commonest and quite often the sole nervous manifestation It may come on in the first fortnight of the disease the so called precocious variety and is disclosed by characteristic nasal voice with or without regurgitation of fluids through the nose On inspection there may be unilateral

or bilateral involvement of the soft palate which hangs limp on phonation and from which the reflex is abolished This precocious type may persist into the fifth or sixth week of the disease and be followed by other nervous sequelae but recovery is usually complete Apart from this form palatal paresis may occur at any time in the first two months of the disease but its duration tends to be limited to a week or two Occasionally the precocious type clears up to be followed by a recurrence of palatal paresis accompanying the later palsies

Oculomotor paralysis usually affects the external rectus of one or both sides and results in convergent squint It may be seen from the third week onwards and lasts for a week or two

Ciliary paralysis resulting in impairment or loss of accommodation also occurs in the third or fourth weeks or later

Facial paralysis usually appears in the fifth or sixth weeks Minor degrees of this are occasionally seen in conjunction with other pareses but well marked unilateral or bilateral forms are not very frequent The expressionless facies of the patient with pharyngeal paresis is often due to concurrent bilateral facial involvement

Pharyngeal paralysis occurs from the fifth to the eighth weeks commonly in the sixth It is sometimes preceded for a day or two by palatal paresis and is frequently accompanied by other palsies The patient at first experiences difficulty in swallowing which is accompanied by coughing and spluttering Deglutition becomes impossible saliva collects in the back of the throat and sets up a reflex cough which is chacteristically guttural The condition lasts from a day or two to a week or two

Respiratory paralysis whilst relatively uncommon must be regarded as a very serious event It is usually preceded by pharyngeal paresis and occurs in the sixth week or after the first sign being a slowing down of the respiration rate The diaphragm is usually affected the abdominal respiratory movements ceasing breathing being carried on by the intercostals and extraordinary muscles of respiration In the unusual event of the intercostals alone being involved chest movements cease respiration being of the abdominal type Whilst certain degrees of paralysis of the respiratory muscles are compatible with survival until recently a high proportion of these cases

succumbed The modern treatment by means of various forms of mechanical apparatus for artificial respiration besides holding out a somewhat improved chance of recovery would indicate as stated by Mitman and Begg (1935) that the *natural duration of the condition is from four to fifteen days* but that the respiratory paralysis may be succeeded by circulatory failure of bulbar origin

Paralysis of *upper and lower extremities* Paralysis of the upper limbs is extremely rare but Ker was of the opinion that paralysis of the lower extremities is probably the most frequent form of paralysis after that of the palate Whilst this is probably true if all degrees of lower neurone lesion are taken into account complete loss of function is very unusual On the other hand in severe cases the knee jerks are often lost the muscles are flabby and tender there is some loss of power various sensory disturbances occur and when the patient gets up he shows an ataxic gait and even some degree of ankle drop It should be noted that the sluggish or absent knee jerks which are frequently the only polyneuritic manifestations in the lower limb of a patient confined to bed may be immediately preceded by a period of increased activity Unless this is appreciated the patient s convalescence may be prematurely speeded up

Paralysis of *the neck and trunk* Occasionally in patients suffering from other forms of paralysis the muscles of the neck are affected so that if the shoulders are raised an inch or two from the bed *the head falls back* When the muscles of the back are involved the patient is unable to sit upright Various muscles in the shoulder girdle may also be affected

Other forms of paralysis which have been observed affect the adductors or abductors of the larynx or the sphincter of the anus or bladder

Complications These are few and since practically every case of diphtheria now receives diphtheria antitoxin a number of patients develop *serum sickness* For a detailed description of its manifestations the section on serum sickness should be consulted *Tonsillitis* and *cervical adenitis* are not uncommon in diphtheria convalescents and the latter may occasionally suppurate *Otitis media*, is also not infrequent An unusual nervous complication is *cerebral embolism* or *thrombosis* resulting

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in hemiplegia but most with an extensive experience of diphtheria have probably met with one or two cases *Embolic gangrene* is also rare but does occur A fair proportion of laryngeal cases are followed by *bronchopneumonia* which is an unfavourable complication after operations for the relief of respiratory obstruction

Associated Diseases Diphtheria and scarlet fever are not infrequently seen as concurrent infections whilst in hospital cross infections of diphtheria in scarlet fever wards are of frequent occurrence Generally these are anterior nasal diphtheria but faucial and laryngeal diphtheria may also be found Some degree of association between diphtheria and measles is also found a laryngitis occurring after the eruptive stage of measles being nearly always diphtheritic

Relapse and Second Attack In our experience relapse in diphtheria is very rare This is somewhat remarkable as over 10 per cent of diphtheria cases are Schick positive on leaving hospital Second attacks and even third attacks may however occur and it would be a mistake to rule out diphtheria in a patient who had previously suffered from a definitely authenticated attack on that ground alone

Varieties of Diphtheria Apart from the anatomical classification already set forth and the assignment of cases to mild moderate or severe groups according to the degree of severity there is only one clinical variety to which special attention need be drawn This is *hæmorrhagic* diphtheria in which in addition to all the signs of the severest form of nasopharyngeal infection with the most profound toxæmia hæmorrhages occur from the mucous membranes and into the skin There is continuous oozing from the throat and nose and indeed severe epistaxis may occur Areas of skin which have been subjected to pressure in the course of treatment *e g* in administering antitoxin or giving hypodermic injections show well marked bruising and in the course of a day or two scattered petechial hæmorrhages appear irregularly distributed over the body Anuria is frequently present and death occurs about the end of the first week

Diagnosis In all cases of illness associated with sore throat or exudate on the tonsils diphtheria should be considered as a possibility and owing to the imperative necessity for com



FIG 6 Post mortem photograph of skin hæmorrhages in case of hæmorrhagic diphtheria They are of two types more or less petechial and large diffuse bruisings The latter occur in the neighbourhood of the elbow flexures and vein and on the chest and followed intravenous and hypodermic injections

within thirty minutes but our experience of the test is that it is by no means reliable a certain proportion of typical diphtheria membranes failing to blacken whilst a definite percentage of exudates due to the streptococcus and other organisms give a positive reaction

In differential diagnosis *tonsillitis* is more often mistaken for diphtheria than any other faucial lesion In the follicular type the pimply appearance of the follicles the great faucial congestion and pain are usually sufficient to make the distinction Some forms of *streptococcal sore throat* including that found in scarlatina simplex show membranous patches on the tonsils which on inspection alone cannot be distinguished from mild faucial diphtheria *Quinsy* is associated with great pain difficulty in opening the mouth and thick speech The throat is much congested the palate bulges on one or both sides while streaks of glairy mucous on the palate and fauces simulate the early gelatinous membrane seen in sharp cases of diphtheria Ulcerative conditions may suggest diphtheria and of these *Vincent's angina* is probably the commonest Indeed it has been said that this more closely resembles diphtheria than any other disease and the sloughy infiltration of the margins of the soft palate or a fragment of craggy tonsil may be misleading Careful observation and swabbing will usually reveal its true nature Chronic ulcerations due to *syphilis* or *tuberculosis* are uncommon in present day fever hospital practice Of recent years we have encountered several cases of *agranulocytosis* which had been provisionally diagnosed as diphtheria These were all of middle age or over and foul extensive ulceration of the fauces accompanied by profound constitutional disturbances were the main features the true nature of the condition only being disclosed by blood examination The *septic type of scarlet fever* after the rash has faded with ulceration on the tonsils and fauces marked enlargement of cervical glands and a pouring nasal discharge may simulate a severe attack of nasopharyngeal diphtheria The history of rash tongue changes the appearance of the patient and the occurrence of scarlatinal complications may help in differential diagnosis It should also be remembered that scarlatina anginosa is relatively rare at present and here again the practitioner will not be content to leave his patient

mencing antitoxin treatment at the earliest possible moment an attempt made to arrive at a clinical diagnosis forthwith The situation of the lesion is important the tonsils uvula, soft palate and anterior faucial pillars being the commonest structures involved The wash leather like appearance of the *membrane with well defined thickened or everted edges* is characteristic Absence of redness of the throat the presence of œdema and relative painlessness are all in favour of diphtheria When an attempt is made to dislodge diphtheritic membrane from tonsils or fauces it only separates with difficulty and leaves a bleeding surface and the fact that it comes away in homogeneous plaques or shreds which sink when placed in water is also helpful In certain cases however when membrane is thin and not extensive or is fragmentary and follicular in appearance it is by no means easy to arrive at a clinical diagnosis If the exudate is not confined to the tonsillar surfaces and the patient is obviously ill in these doubtful cases the only wise course is to isolate the patient administer antitoxin and await the result of bacteriological examination of nose and throat swabs A great many doubtful cases however apart from a limited amount of exudate in the throat show little sign of systemic disturbance and in these it is justifiable to perform a Schick test and delay the intramuscular injection of antitoxin for four hours By this delay there will be no interference with the Schick test and Mayfield (1934) has shown that even employing an interval of two hours between test and serum the Schick test can be relied upon A negative reaction will rule out diphtheria for all practical purposes whilst a case of diphtheria will show a positive reaction The latter result however does not in itself indicate diphtheria unless the appropriate bacteriological results are also obtained For a complete and comprehensive diagnosis of diphtheria therefore the clinical appearances should be typical or at least suggestive the patient should be susceptible to the disease as shown by a positive Schick test and a virulent strain of C diphtheriae should be isolated from the lesion

It has been suggested by Manzullo (1938) that the diagnosis of diphtheria may be assisted by the swabbing of the suspected throat membrane *with 2 per cent potassium tellurite solution* Diphtheria membrane becomes sooty black in appearance

especially when measles is epidemic will do much to eliminate error but there is no clinical sign to guide the practitioner in whooping cough Direct examination of the larynx and negative bacteriological findings will exclude diphtheria whilst cough plates will reveal B pertussis in a high proportion of cases *Retropharyngeal abscess* may also be mistaken for laryngeal diphtheria on account of respiratory stridor but careful inspection and digital examination will usually make the diagnosis clear *Foreign body* in the larynx may also give rise to signs simulating diphtheritic laryngitis and whilst direct laryngoscopic examination will usually rule out this condition the issue may not be put entirely beyond doubt e g a piece of grape skin impacted in the larynx has offered a passable imitation of diphtheria membrane On two occasions *suppurative mediastinitis* has come under our notice provisionally diagnosed as laryngeal diphtheria owing to pressure on the trachea causing dyspnœa In one instance drainage resulting in recovery was established when the skin incision for tracheotomy was performed whilst in the other the diagnosis was only forthcoming at autopsy *Laryngismus stridulus* when seen in the severe form in ricketty infants may present difficulty Also severe attacks of *broncho pneumonia* are not infrequently sent in to hospital as cases of laryngeal diphtheria on account of cyanosis rapid laboured respiration and slight indrawing of the intercostal spaces but the chief signs of laryngitis are wanting Anterior nasal diphtheria requires little mention in differential diagnosis It should be the first thing thought of in children with intractable nasal discharges of the type already described in connection with this condition

Bacteriological Diagnosis Whilst it is true that ultimately the diagnosis of diphtheria rests on the isolation of the specific organism from a lesion in a susceptible person and on occasion bacteriological examination gives results otherwise unobtainable it should be realised that the practitioner can never transfer even a small part of his responsibility for diagnosis to the bacteriologist Direct smears from diphtheritic lesions yield a high proportion of positive results in the hands of experienced workers and while the rapid provisional result thus obtainable may be useful for example in institutional

untreated by antitoxin whilst bacteriological aid is sought It should hardly be necessary to mention the subject of *mumps* in connection with the differential diagnosis of diphtheria but we have unfortunately to record every year several severe and sometimes fatal cases sent into hospital with that diagnosis when even a brief examination of the fauces would have revealed the true nature of the illness Since the operation of tonsillectomy has become relatively common it may be a matter of some difficulty to distinguish between the sloughs resulting from that operation and diphtheria Diphtheritic infections of tonsillectomy wounds are by no means unknown and moreover tend to be severe so that the necessity for making the distinction may be urgent The *tonsillectomy slough* assumes from the first the shape of the tonsillar bed and is restricted to that site though occasionally the faucial pillars and uvula receive slight attentions from the instruments of the surgeon which cause small yellow sloughs sometimes mistaken for membrane The anxieties resulting from this clinical problem would be abolished for all practical purposes if the patient were Schick tested and actively or passively immunised beforehand In male babies *thrush* is sometimes mistaken for diphtheria but the latter is uncommon below the sixth month and in thrush the buccal mucosa is usually affected a very rare site for diphtheria Sometimes also mistaken for diphtheria are the small discrete yellow sloughs on the tonsil due to *herpes faucialis* while an early *chickenpox* lesion in the same situation may also lead to the same error The commonest condition simulating laryngeal diphtheria is *streptococcal laryngitis* which may produce signs of obstruction indistinguishable from those of the diphtheritic variety if there is no clue to the nature of the infection in the shape of diphtheria membrane in throat or nose Faucial membrane even when atypical or limited in amount points almost certainly to diphtheria but if this is absent the only method likely to give immediate assistance in diagnosis is direct laryngoscopy by which membrane is seen on the epiglottis or larynx Other forms of acute laryngitis with obstructive signs are found in the prodromal stages of other infectious diseases notably *measles* and *whooping cough* In the case of the former a routine examination for Koplik spots and evidence of catarrh

with the medium care being taken to avoid breaking up the surface

Prognosis In general terms this depends on the type and severity of the attack the age of the patient and the day of disease on which specific treatment is commenced With regard to clinical type hæmorrhagic diphtheria is practically always fatal It is to be noted also at the present time that the great majority of diphtheria deaths occur in those suffering from the severe nasopharyngeal form of the disea e and at the North Western Hospital cases so classified on admission showed a fatality of practically 40 per cent Laryngeal diph theria also carries a grave prognosis we venture to think improved of recent years by the introduction of endoscopic treatment but any series of cases requiring operation may show a 10 to 50 per cent mortality The age of the patient is moreover a most important factor in prognosis over 70 per cent of our diphtheria deaths occurring in children of six years or under Also clinical experience points conclusively to the fact that prognosis worsens steadily the later the stage in the disease the patient receives antitoxin Recently medical statisticians have been disposed to criticise the statistical evidence advanced in favour of this by clinicians and it is possible that some of it will not stand up to modern methods of statistical analysis but for what it is worth we propose to mention that of all deaths from diphtheria at the North Western and Edinburgh City Hospital from 1931–45 inclusive viz 374 256 or 68 44 per cent received antitoxin on the fourth day of disease or after In individual cases those *which can be classified as anterior nasal or faucial will do well* although in the latter if membrane is fairly extensive con valescence may be interrupted by the occurrence of one or more of the pareses The probability of recovery of the severe nasopharyngeal case has already been expressed statistically but in calculating the chances of recovery of the individual case it is difficult to provide any definite rules and often progress must be measured in terms of the daily estimate of the patient s condition If the infecting strain of C diphtheriae is known it is important to remember that gravis and inter medius infections between them account for all but a few of our diphtheria deaths at present According to Harries (1938)

outbreaks and might be employed more often than it is where facilities are available it can only be of value when a positive result is obtained In routine work the results of culture are awaited before final reports are given This means however the loss of time as far as treatment is concerned and it is this delay which may make all the difference between success and failure Furthermore it is within the experience of everyone that from time to time cultures from typical diphtheria will *yield negative results positive results being obtained only* after repetition of the culture and while many are content to rule out the diagnosis of diphtheria on two successive negative cultures our own routine practice for this purpose is to seek three negative cultures taken on the first three days of admission to hospital Finally it should be borne in mind that the diphtheria bacillus may be isolated from a patient in which the lesion is due to some other organism *e g* streptococcal tonsillitis occurring in a diphtheria carrier so that the results of swabbing will often require to be correlated with simultaneous Schick testing With these limitations of bacteriological examination in mind therefore the prudent practitioner will not hesitate to give diphtheria antitoxin when the clinical appearances in any given case indicate even the possibility of diphtheria In taking swabs certain precautions must be observed if the best results are to be obtained The swab should not be taken when antiseptics have been recently applied to the throat The child will usually require to be held firmly and the swab should be firmly pressed over the exudate and the surface of the tonsils fauces and post pharyngeal wall The L C C Departmental Committee recommended that when post nasal diphtheria is suspected the terminal ½ or ¾ inch of the wire carrying the swab should be bent at a suitable angle so that when the tongue is depressed it can be passed behind the soft palate and rubbed over the posterior wall of the naso pharynx In nasal diphtheria the swab should be introduced along the floor of the nose as far back as possible If culture medium usually Loeffler in routine work is to be immediately inoculated the practitioner should discard dry medium and only employ culture tubes showing a little water of condensation at the bottom The swab should be rubbed firmly over the surface and rotated so that every part of it comes into contact

associated with that form of the disease When operation is necessary caution should be observed in prognosis and if broncho pneumonia ensues the outlook is most grave

Prophylaxis The main general measures are notification isolation and disinfection but as in the case of scarlet fever it cannot be said that these have had much effect in limiting the spread of infection in diphtheria Since adequate treatment is only possible in hospital or in specially good home surroundings the policy of hospital isolation of practically all cases is usually adhered to Cases of anterior nasal diphtheria and carriers are sought for amongst contacts and very considerable importance should be attached to the former since they are responsible for the spread of infection in a great many cases particular y in children of school age With regard to the search for contact carriers the indiscriminate swabbing of all and sundry and hospitalisation of those giving a culture containing organisms morphologically resembling the diphtheria bacillus is now generally deprecated The bacteriological examination of cultures from contacts should be carried through to the virulence test and correlated with the results of Schick testing of the individuals concerned Until these results are forthcoming contacts should be kept under clinical observation and at the first suspicion of diphtheria should be treated as such Those with positive Schick tests and virulent cultures may be incubating the disease and in the absence of clinical signs should be given a small dose of antitoxin whilst those with positive Schick tests and negative cultures should be re swabbed and kept under observation until a second negative is obtained Those with negative Schick tests and negative cultures need not be further considered but those with negative Schicks and giving virulent cultures are true carriers requiring further observation and treatment as outlined below In localised outbreaks it is also customary to investigate milk supplies Specific methods of immunisation against diphtheria are now available and as a result of the comparative failure of general measures it is to the wide application of these that we must now look for any considerable success in diphtheria prevention

Passive Immunisation When diphtheria suddenly appears in a family or institution it may be necessary to obtain the

reliance in prognosis can be placed on the blood sugar curve In diphtheria sugar tolerance curves are of the diabetic type and the greater the lag the worse the prognosis In the absence of facilities for these estimations the practitioner will depend on such observations as the early onset of palatal paresis which is frequently accompanied or followed closely by circulatory failure and the behaviour of the pulse rate and heart sounds As Leete (1938) has pointed out much of value in prognosis can be learned by a systematic study of these In his view the myocardium is severely affected when there is a steep fall in the pulse rate within the first week with diminution of the first sound and the presence of extra systoles and albuminuria Here heart recovery will depend on increase of pulse rate without reduplication of the sounds but if recovery takes place severe paralysis may ensue When the myocardium is fatally affected there is also a steep fall in pulse rate to 40 or below the first sound is diminished or inaudible there are numerous extra systoles reduplication of the sounds and heavy albuminuria In our experience also in cases of circulatory failure associated with sudden collapse or with vomiting and precardial pain the outlook is ominous Patients who recover from severe degrees of circulatory involvement usually show no permanent impairment of function and Alstead (1933) who has carried out electrocardiographic investigation of cases previously suffering from diphtheria found nothing to suggest gross cardiac lesions in them Nevertheless there may be a persistence of irregularities and the possibility of fibrosis of the heart wall In the various palsies complete recovery is the rule but when the condition is generalised and pharyngeal paralysis appears the outlook is serious Like the others this tends to pass off but as long as it persists there is always the danger of an aspiration pneumonia and also it is often the forerunner of a respiratory paralysis Until recently the prognosis in the latter has been poor but it is now believed that the situation has been somewhat improved by the introduction of mechanical respirators such as the Drinker and Bragg Paul apparatus In laryngeal diphtheria once obstructive signs have disappeared the patient should do well but if this is secondary to nasopharyngeal infection the patient will have to encounter the hazards

reactors at this age are uncommon At all other ages and in re testing after active immunisation both test and control should be performed

Since active immunisation was introduced there have been gradual improvements in the antigen immunologists having sought to produce reagents which will produce the maximum response with the minimum number of injections and with the minimum amount of unpleasant reaction At first *toxin antitoxin* (*T A*) *mixtures* were employed but in the United Kingdom they were rapidly superseded by *toxoid antitoxin* (*T A M*) *mixtures* toxoid being a derivative of toxin formed by the action of formalin a process which to a large extent destroys toxicity but leaves unimpaired the specific antigenic properties Later a considerable amount of immunisation was carried out with toxoid itself or *formol toxoid* (*F T*) as it is usually termed It has been shown to be a highly efficient prophylactic and as it contains no antitoxin is free from the possible objection that it may sensitise the immunised individual In a certain proportion of cases especially adults it may give rise to sharp local and general reactions but for routine work in young children it will be found highly satisfactory To overcome the difficulties caused by reactions in older children and adults Maloney and his co workers (1927) devised an intradermal test for detecting sensitives but there have been conflicting views on its significance (Swyer 1935 Mitman 1936) and most workers are content to protect older children and adults with *toxoid antitoxin floccules* (*T A F*) a suspension in saline of the precipitin obtained by the interaction between toxoid and antitoxin This is an excellent prophylactic It has a high antigenic value and since it contains only a trace of nitrogenous material it is practically free from troublesome reactions The prophylactic which is most extensively used at present is *alum-precipitated toxoid* (*A P T*) This was introduced by Glenny and his co workers (1926) and was made by adding alum to formol toxoid thus producing a highly insoluble substance which of all the prophylactics shows the highest antigenic efficiency It suffers from the disadvantage that it tends to produce sharp local and general reactions and some of the earlier samples in our own experience in several instances produced small cold ab cesses but judging from the results

immediate protection of contacts without waiting for the results of Schick testing and swabbing as described above An effective temporary immunity lasting for about three weeks can be obtained by the injection of from 500 to 2 000 units of diphtheria antitoxin but it should be realised that if this method is employed in institutional outbreaks the obligation to seek out undisclosed sources of infection is in nowise diminished as unless this is done at the end of the period of temporary immunity further cases are likely to appear

Active Immunisation Amongst the staffs of fever hospitals and institutions active immunisation against diphtheria has given convincing proof of its efficacy It has also been employed on an extensive scale among urban populations in the United States and Canada and as an example of what can be achieved the results in Toronto reported by Fitzgerald *et al* (1938) may be quoted *For over thirty years prior to the commencement* of active immunisation morbidity rates had shown no definite decline and in 1930 were 164 per 100 000 of the population Following prophylactic inoculation among school children by 1935 the morbidity fell to 3 5 per 100 000 From the early twenties the procedure was carried out in a more limited fashion in a number of the large towns of the United Kingdom and came to be numbered among the routine activities of local authority public health departments While individuals undoubtedly benefited little impression was made on the general diphtheria morbidity and mortality but since a really intensive campaign sponsored by the central health departments was initiated in 1941 the results have been striking particularly in reducing mortality among the immunised population In Scotland for example in the years 1941–44 inclusive there were 1 049 deaths among the non immunised section of the school and pre school population as compared with twenty seven among the immunised the latter forming the preponderance of the school and pre school population

Active immunisation should be carried out as early as possible after the first birthday and since practically all children at that age are susceptible to diphtheria preliminary Schick testing may be omitted the same applying to those up to the age of five From five to fifteen the Schick test may be carried out, but the control need not be applied since pseudo

from 1923 we doubt however if it is wise to rely too greatly on this hypothesis having seen severe and even fatal diphtheria in children immunised to the Schick negative state a number of years previously *Re immunisation* is therefore of first class importance and we are in agreement with Parish and Wright (1935) that even natural Schick negatives be given one injection of prophylactic at the time of the Schick reading and that in addition it is advisable to give periodic injections to all whether Schick negative on primary test or after a course of immunisation so that a high degree of immunity may be maintained *Schemes for diphtheria protection on a large scale should envisage re immunisation as well as primary immunisation* a course of inoculations being repeated just before school entry and at any subsequent period should exposure to diphtheria become a possibility Following one or other of the immunising injections a certain proportion of individuals usually adults will show a variable amount of *local reaction* in the shape of redness and induration at the site of injection and occasionally a *constitutional reaction* including pyrexia malaise and headache These last only a day or two and produce only temporary discomfort

Very promising results are claimed for a period of combined passive and active immunisation by Fulton Taylor Wells and Wilson (1941) who report the prompt termination of a number of outbreaks of diphtheria in closed and semi closed communities immediately it was applied Without preliminary Schick testing all at risk were given 0 3 c c alum precipitated toxoid in one arm and 500 units of refined antitoxin in the other All were swabbed at the same time and the positives segregated Four weeks later all received a second injection of 0 3 c c of alum precipitated toxoid After an interval of a further two weeks carriers were released from isolation and allowed to mix freely with the others It is important to note that all new comers must be actively immunised before entering the community or kept apart until this is completed

Treatment This may be summarised under the headings of general management specific treatment the treatment of sequelæ and complications and the special requirements of laryngeal diphtheria For details of the method of home isolation the section on scarlet fever should be consulted

in the large numbers of children inoculated in the last few years very little in the shape of unpleasant results is to be apprehended At first there was some evidence (Saunders (1937)) that even one injection gave a high proportion of Schick negatives but subsequent experience has discredited this method of one shot immunisation To obtain a satis factory immunity level which will be durable two injections of 0 2 and 0 5 c c at an interval of three to six weeks is necessary If formol toxoid toxoid antitoxin mixture or toxoid antitoxin floccules are employed a course of three injections of 1 c c each should be given subcutaneously or intramuscularly with a three to six weekly interval between there being strong evidence that with the longer interval the probability of reaching the Schick negative state is enhanced A method of immunisation by *intranasal instillation* of a purified aluminium hydroxide toxoid was recommended by Jensen (1937) but this has not made much headway possibly because of undesir able upper respiratory infections as described by Andersen (1939) By whatever method immunisation has been attempted when two or three months have elapsed since the last immunising injection the Schick test and control should be performed in a representative sample of those inoculated to assess the results of immunisation and in those likely to be exposed to special risk *e g* fever hospital nurses re testing should be carried out in all cases This is necessary because a varying proportion of individuals from 5 to 15 per cent may *remain Schick positive* but a further *injection or course* of injections will usually be found to produce the required effect In the earlier days of immunisation it was customary to regard diphtheria immunity induced by active immunisation as practically permanent Parish and Okell (1928) finding that only 5 per cent of artificially immunised children and 1 0 per cent of naturally immune children relapsed to Schick positive one to seven years later Dudley (1934) found a relapse rate of nearly 10 per cent but believed this feature of immunisation to be of little consequence the body once having been trained to respond to the specific stimulus reacting rapidly to the stimulus of infection even if the antitoxic titre of the blood has fallen below the Schick immunity level From our practical experience of field immunisation in Edinburgh which dates

the disturbance of function characteristic of the various palsies Reading for those so inclined need not be prohibited but in view of the possibility of ocular pareses should be in moderation

Specific Treatment There is abundant evidence of the efficacy of serum treatment in diphtheria and while the continuous fall in the case fatality rate which has taken place during the last forty years cannot be claimed by even the most enthusiastic to be entirely due to the introduction of antitoxin nevertheless those who have had the opportunity of watching its effects in individual cases in severe naso pharyngeal and laryngeal cases cannot fail to be impressed by its action It should be realised however at the outset of any discussion on this subject that the administration of antitoxin in diphtheria is a method of passive immunisation and that its action therefore is but little retrospective In a pronouncement on this subject a London County Council Committee on The Dosage of Antitoxin in Diphtheria (1936) state that all the evidence points strongly to the view that toxin firmly united to the living cells is entirely uninfluenced by antitoxin This explains the urgent necessity for commencing treatment at the earliest possible moment It is also of importance that the *dose of antitoxin* should be adequate and in assessing the severity of the case with a view to determining dosage various factors require to be taken into account With regard to the local lesion the more extensive the membrane the more severe is the case and poorly defined semi translucent membrane may indicate a greater degree of severity than well defined membrane The degree of faucial œdema the presence of fœtor and the amount of adenitis or periadenitis will all require consideration in assessing the severity of the attack particularly the last mentioned as the presence of periadenitis will sometimes point to a severe case when other signs are equivocal In addition to the extent and character of the local lesion toxæmia as disclosed by prostration drowsiness pallor and albuminuria must be estimated Age and body weight are generally disregarded in this country but it is usual to make some allowance for duration of disease before the commencement of specific treatment late cases receiving larger doses than apparently similar cases at an earlier stage although

General Management The keynote of this is the maintenance of the recumbent position and the complete avoidance of all effort At first the patient should be given only one thin pillow all movement and sitting up in bed being strictly forbidden Daily soap and water enemata should be administered and the output of urine measured and tested for albuminuria Spoon or cup feeding should be carried out Owing to the condition of the throat the patient will be at first on a milk diet but this should be supplemented with 3 to 5 ozs of glucose per diem dissolved in water and flavoured with fruit juice As soon as the throat permits and in all except the severe cases this will not be more than a few days the diet should be increased by milk puddings ice cream egg flip custards jellies potatoes mashed with gravy or butter pounded fish or minced chicken Local treatment of the throat has now largely been abandoned except when there is necrotic membrane or superadded septic infection when flushing of the throat with sodium bicarbonate solution 6 grs to the ounce three or four times daily will help to clean away debris In mild or moderate cases a second pillow may be given at the end of from ten days to three weeks and in the course of another week a third pillow The patient is next permitted to sit up in bed for a short period and the process is gradually extended until about the fifth or sixth week he may leave his bed to rest on a reclining chair or sofa Then a few steps about the room are allowed and finally at the end of two months he should be taking short walks In the mildest cases the above programme can obviously be speeded up but on the other hand in severe cases which have showed well marked toxæmia or when the cardiac complications have occurred it is wise to keep the patient flat for seven or eight weeks and in bed for about twelve In every instance with each successive advance from the recumbent posture the most careful watch should be kept for variations in pulse rate or rhythm faintness or nausea and at the slightest sign of these the patient may require to be put back one or more stages Careful nursing is essential the various nursing operations such as bed bathing and toilet of the mouth being performed with the maximum of gentleness and a careful watch must be kept for early signs of pulse irregularities and

serum dosage and for mild cases 2 000 to 10 000 units for moderate cases 15 000 to 30 000 and for severe cases 50 000 to 100 000 units of diphtheria antitoxin should be given The patient should be re-examined after twelve or twenty four hours and the position again reviewed If membrane and toxæmia are more extensive than originally supposed a recon sideration of dosage is called for and in such cases it is wise to give the full dosage on the new assessment of severity the fact that serum has already been given being discounted While numerous clinical observations bear out the view that little benefit is likely to follow the administration of serum after the fifth day of disease it should be clearly understood that antitoxin should always be given however late and however hopeless the case

The *method of injection* is of secondary importance only to the dose of antitoxin Since by the *subcutaneous* route the maximum concentration of antitoxin in the blood is only reached after forty eight to seventy two hours there is no reason why its employment should be continued The *intra muscular* route gives three to six times more rapid absorption and for all doses up to 20 000 units the injection should be made into the vastus lateralis Patients who require a greater dosage should have the serum given *intravenously* and this route is of particular importance in all severe cases Should the intravenous route be impossible and this is occasionally the case in small children with collapsed veins and marked toxæmia the *intraperitoneal* route is a useful alternative since it gives more rapid absorption than by intramuscular injection This is carried out with the ordinary syringe and needle the latter being introduced through the anterior abdominal wall in the midline 1 or 2 inches below the umbilicus The pre cautions to be observed in serum administration will be found in the section on serum sickness

The various commercial sera now on sale are invariably concentrated until recently each cubic centimetre containing about 2 000 units of antitoxin while specially potent con centrations were available containing 3 000 units A still higher degree of refinement and concentration has however now become possible by means of a process of digestion so that there is available from ordinary commercial sources diphtheria

it is to be assumed that if the lesion is progressive the greater extent of membrane and toxæmia would call for a larger dose in any event Since it is believed that a single dose of serum administered at the outset gives a higher and earlier con centration of antitoxin in the blood than the injection of successive fractions whose total is the same an effort should be made to assess the requirements of the case at the beginning This is done by grading the severity of the disease according to the factors above mentioned and though systems of classification for the purpose of serum dosage have been recommended which are somewhat minutely worked out it is doubtful if anything is gained by the elaboration of clinical details into differential criteria by which many degrees of severity may be established We are of the opinion that a satisfactory classification for purposes of serum dosage should *be simple and based on what experience suggests will be the* outcome of illness when adequately treated The art of prognosis in diphtheria cannot be expected to do much more than indicate which of three main courses any given case will follow First there is the mild case in which the local signs of infection will rapidly disappear convalescence will be short and uncomplicated and the risk of death nil Secondly there is the case of moderate severity in which the local signs of infection will be overcome in a few days but there is the possibility that convalescence may be marked by the occurrence of one or other of the later sequelæ but again the risk of death is nil Thirdly there is the severe case in which the outcome as far as survival is concerned is uncertain or if recovery ensues it may be marked by complications or sequelæ in themselves occasionally dangerous and necessitating a prolonged convalescence Mild cases will include those previously designated *as anterior nasal and the slighter cases* of the faucial type Moderate cases will include the faucial type with more extensive membrane and the less urgent cases of the laryngeal type The severe type will include all naso pharyngeal cases including those in which signs of laryngeal involvement are present Extra respiratory lesions are variable in their severity but in our experience it is advisable to treat such cases as moderate or severe The above classification of clinical severity was that adopted by the L C C Committee on

ground that on first inspection the full extent of the filmy membrane has escaped detection The edges of the membrane eventually *beome thickened and everted* in a day or two it becomes discoloured and detached so that considerable pieces may be expectorated By this time in a favourable case nasal discharge has practically ceased the periadenitis has resolved swallowing is much easier from the subsidence of faucial œdema and the patient has regained some of his alertness By the end of a week or ten days there may be little to be made out on inspection of the throat except rawness over the site of the membrane or possibly some traces of sloughy exudate on the tonsils or post pharyngeal wall Patients coming late under treatment do not show the same response Membrane œdema and capillary oozing from nose and throat persist resolution of cervical adenitis and periadenitis is delayed and the patient remains in his toxæmic lethargy until the onset of early cardiac complication

Penicillin Therapy On the basis of experimental work *in vitro* C diphtheriæ has been found sensitive to the action of penicillin but in our personal observations on its use in severe nasopharyngeal cases we have not found that it exerts the slightest influence on the course of the disease whether applied to the local lesion in the form of lozenges or sprays or by the continuous intramuscular drip This is perhaps somewhat disappointing but it is what might have been expected from our conception of diphtheria except possibly in the laryngeal form as a disease in which damage results from toxin fixation in the tissues prior to the patient coming under treatment

Ancillary Methods of Treatment of Toxæmia In severe toxæmia some benefit may be brought about by the adminis tration of glucose Following the work of Schwentker and Noel (1930) Benn and his co workers (1932) advocated giving insulin as well but more recent work by Begg and Harries (1935) has indicated that there is no advantage to be derived from insulin Glucose administration should be initiated at the onset of treatment by combining it with the intravenous serum necessary in a severe case our practice being to run in by the drip method 1 to 3 pints of 5 *per cent* glucose *in saline* at the same time as the antitoxin is given Benn recommends that thereafter 100 to 200 grms of glucose should be given

antitoxin which contains as much as 8 000 units per cc This has the advantage that the administration of large amounts of serum is facilitated while the incidence of serum reactions is much reduced As all diphtheria antitoxin on sale in the United Kingdom must conform to the standards of potency and sterility laid down in the regulations made under the Therapeutic Substances Act, 1925 the practitioner may rest assured as to the quality of any antitoxin he may be supplied with

The subject of antitoxin administration in diphtheria cannot be left without some allusion to the fact that unanimity on dosage is by no means complete The scheme of dosage set forth above was adopted by the Committee concerned as providing a sufficiently elastic range to permit of its acceptance by as large a body of authoritative opinion as possible Some, however such as Ker Goodall and Park believe that all the benefit which can be expected from diptheria antitoxin may be obtained by maximum doses of 50 000 to 60 000 units Of recent years however and especially following the work of Bie (1922) there has been a widespread tendency to increase the dosage very greatly so that at the present time in severe cases 100 000 to 200 000 units or even more are given intravenously by some So far as our own clinical observations go we have seen no reason to adopt the latter system in preference to that described but it should be clearly understood that, within the ordinary range of dosage an excess of antitoxin can do no harm and the practitioner in doubt as to whether he should give a larger or a smaller dose should unhesitatingly decide on the former

In mild and moderate cases the most obvious effect of serum is the rapid disappearance of membrane which occurs within twenty four or forty eight hours after injection In severe cases there may be little or no immediate change visible in the local or general condition but in from twelve to twenty four hours especially if antitoxin has been given intravenously at an early stage drowsiness is less marked faucial œdema recedes and membrane has undergone delimitation Indeed in severe cases treated early the membrane may actually appear to have spread in the face of even the heaviest doses of antitoxin but this sometimes can be explained on the

Paralyses These proceed to spontaneous recovery and as a rule need little treatment beyond tonics and rest In palatal paresis owing to the patient s tendency to regurgitate fluids through the nose semi solids should be given In pharyngeal paralysis feeding by the nasal tube should be resorted to early care being exercised to prevent aspiration of food into the larynx otherwise a septic broncho pneumonia may be set up The foot of the patient s bed should also be raised to allow saliva and mucus to drain away To prevent the collection of this in any quantity in the back of the throat a suction pump actuated by a small electric motor and attached to a soft rubber catheter is very helpful suction being applied periodically Respiratory paralysis is a hopeless condition unless early admission to a hospital equipped with a Drinker or Bragg Paul apparatus can be obtained and should either of these be available no time should be lost in getting the patient under treatment We have had the opportunity of using both forms of apparatus mentioned in this condition and both have proved successful in maintaining respiration in cases which otherwise would have succumbed It should be realised however that even if mechanical methods are capable of maintaining respiration there is a definite tendency to the development of pulmonary œdema and hypostatic pneumonia while heart failure occasionally nullifies the successful application of the respirator In severe cases of generalised paralysis in which the lower extremities or other groups of skeletal muscles are involved massage and passive movements will help in accelerating the return of function

Complications Tonsillitis adenitis and otitis media occurring in the course of convalescence are treated on ordinary lines For the treatment of serum sickness attention is invited to the section dealing with this subject

Laryngeal Diphtheria In all cases of laryngeal diphtheria the first step in treatment is to give an adequate dose of antitoxin The practitioner confronted with a case for which hospital facilities are not available will combine this with expectant treatment and tracheotomy if necessary Until a *few years ago with the exception of indirect intubation* hospital practice had little to offer in the shape of refinements in treatment beyond these but more recently important methods

daily by the mouth in lemonade or if this becomes impracticable by reason of nausea 40 to 100 grms in 50 per cent solution are injected intravenously until it can be taken by the mouth again Glucose requires therefore to be given freely for two or three weeks in severe cases Working on the assumption that the toxæmia of diphtheria leads to damage of the suprarenal gland shown during life by the signs of suprarenal cortex deficiency Maclean (1936) claims success in treatment of severe cases by the administration of sodium chloride intravenously by the mouth and continuously into the rectum Employing large doses of extract of suprarenal gland cortex however we have been unable to note any beneficial effect

Heart Failure At the first sign of this the foot of the bed should be elevated Vomiting and pain require the application of frequent hot fomentations to the region of the heart and all feeding by the mouth stopped thirst being alleviated by moistening the lips and tongue with iced water Rectal salines and intravenous glucose should also be tried if the latter can be given without much disturbance to the patient Every drug with any reputation as a cardiac stimulant has been employed but with little success In common use are alcohol ether strychnine camphor caffeine coramine atropine ephedrine adrenalin and pituitrin If restlessness is marked small doses of morphine may be cautiously given Friedemann (1934) has recommended hot baths as helpful in the vasomotor collapse in diphtheria the patient being carefully conveyed in a sheet to a bath at 105 –110° F and immersed for ten to thirty minutes The traditional treatment of diphtheria in this country would probably render clinicians cautious in applying this method but we have on occasion tried this line of treatment in a modified form namely the application of the hot air bath at temperatures up to 105 F a temperature which according to Heald (1935) should not be exceeded It is not claimed that the benefit is more than temporary but in several cases we have seen a striking improvement in colour and in the comfort of the patient and it is conceivable some patients may be tided over a critical period In patients who have recovered after showing cardio vascular signs and symptoms during the attack it is well to forbid all strenuous exercises for a year after the illness

secure a successful result without operation When the patient is in hospital therefore and skilled assistance is at hand to perform operation at a moment s notice the case can be persevered with well into the spasmodic stage a careful watch being kept on the pulse At the first sign of flagging operation is indicated A general anæsthetic such as chloroform may be given when the operation is performed in private practice but if time permits a local anæsthetic is preferable Frequently the urgency is so great that the operation will have to be done without anæsthesia and indeed many dispense with an anæsthetic in all circumstances mainly from a desire to avoid interference with the cough reflex The patient is wrapped tightly in a blanket to control the arms and legs and placed on a table with a rolled up sheet under the shoulders The head must be held by an assistant so that the median plane is exactly at right angles to the floor and this position must be maintained until the trachea is incised Before commencing operation it is a wise precaution on the part of the operator if he does not usually wear spectacles to provide himself with a pair of plain glasses to protect the eyes The skin having been prepared the position of the cricoid cartilage should be established the second finger and thumb being placed on each side of the larynx and the index finger on the middle of the lower border of the cricoid Throughout the operation the left hand should not move from this position The incision is made downwards from the lower border of the cricoid for an inch or an inch and a half care being taken that the incision does not tail off to one side or the other Dissection should then be made through the various tissues until the rings of the trachea are recognised if necessary the isthmus of the thyroid gland being cut through and ligatured with artery forceps During dissection venous oozing may occur but this should be met by swabbing rather than the application of forceps When the trachea is reached the laryngologists strongly recommend that the second and third rings should be incised so that the intact first acts as buffer between the tracheotomy tube and the laryngeal cartilages In this way the danger of subsequent laryngeal stenosis is said to be diminished On opening the trachea there will be immediate expulsion of blood stained frothy mucus and the patient

in the diagnosis and treatment of this condition have been developed as a result of the application of endoscopy Cases in which obstructive signs are not well marked are examined by direct laryngoscopy diagnosis being further facilitated by taking a direct swab from the larynx, and this followed by expectant treatment will be all that is necessary If obstructive signs are more advanced after inspection and taking cultures from the larynx aspiration and re-aspiration of membrane and mucus from the larynx and trachea will be undertaken to supplement expectant treatment Should this fail to give relief direct intubation by way of the laryngoscope will be required These various methods will now be considered in detail

Expectant Treatment If signs and symptoms indicate the initial stage of laryngeal obstruction the patient should be placed in a half tent constructed by placing a screen round the head of the bed and roofing it over with a sheet which also projects down in front for about one third of its height from the top Into this is led steam from a bronchitis kettle, or from the steam jet which is provided in many fever hospitals The steam should be adjusted so that a gentle current warms and moistens the air breathed by the patient and it is the practice of some to tie a few layers of gauze soaked in Tinct Benzoin Co over the mouth of the jet Frequent hot fomentations are applied to the neck and we administer a mixture of Tinct Belladonna minim iv Tinct Camph Co minim vii with water 1 drachm for its antispasmodic effect in full doses of 1–1½ drachms Careful and assiduous nursing is most essential and the practitioner should visit as frequently as possible to see how the patient is responding to treatment Also as the onset of a sudden emergency such as the occlusion of the airway by detachment of a piece of membrane is always a possibility he should be within easy call

Tracheotomy If when first seen the patient is obviously in the spasmodic stage or in spite of expectant treatment this has been reached and hospital facilities and experienced nursing are not available the practitioner has no option but to operate In hospital expectant treatment can be persevered with further *for all who have experience of this condition* however confident in their operative ability would prefer to

be necessary for the night following removal In a successful case the wound heals quickly with surprisingly little scar tissue Should signs of respiratory obstruction follow the withdrawal of the tube it should be replaced but daily attempts must be made to get it out The main obstacle to this in some children is psychological but organic obstruction due to granulations above or below may be the cause In the latter case the introduction of a larger tube may remove the difficulty but when granulations are above the wound delay in seeking the aid of the laryngologist should not be incurred lest complete laryngeal stenosis result This unfortunate sequel in our experience has almost invariably been the result of damage caused to the cricoid cartilage by an inexperienced agitated operator and it is fortunately a very uncommon sequel to operation in hospital practice Indeed the laryngologists assure us that it would be practically unknown if the tracheal incisions were kept below the first tracheal ring and Jackson (1934) advises that incision should be through the third fourth and fifth rings To this we would add the exhortation to get the tube out at the earliest possible moment Broncho pneumonia may follow tracheotomy within a day or two of operation and should be treated on the usual lines

Indirect Intubation Until the event of endoscopic methods in the treatment of laryngeal diphtheria the choice of operation in hospital practice lay between tracheotomy and indirect intubation Both operations had their adherents and neither is mutually exclusive but it is probably true that in this country tracheotomy was regarded as the operation of choice by the majority of fever clinicians whilst in America the opposite is the case It should be noted however that such authorities as Ker and Goodall have expressed their preference for intuba tion and in our view in the hands of a reasonably skilled operator there is little relief to be obtained by tracheotomy in any form of laryngeal diphtheria which cannot be equally secured by intubation The latter causes less shock can be performed very rapidly and once the necessary dexterity is gained is much easier It probably requires a much greater degree of devotion on the part of the medical man in attendance and more skill on the part of the nurse but we have never had the slightest difficulty in training the modern fever nurse in

should be allowed to cough the upper air pasasages clear before the tracheotomy tube is put in place To prevent the aspiration of blood at this stage the head and neck should be lowered below the level of the body A suitably sized Parker s tube made of sterling silver with fenestra in the shoulders of both inner and outer tubes is then inserted A tube fitting fairly closely to the trachea is to be preferred It is then tied in position with a layer of boric lint between the shield and the skin The patient is returned to bed and kept in the steam tent for at least twenty four hours after operation

While the immediate results of tracheotomy are frequently spectacular the remote results which ultimately depend on the successful removal of the tube must be considered The after care consists in the careful supervision of the patient and the inner tube which must be removed every few hours and thoroughly cleaned out in a solution of boric acid and sodium bicarbonate each ½ oz to the pint The outer tube should not be removed except in an emergency but if a sudden obstructive attack occurs it must be withdrawn and laryngeal forceps inserted in an attempt to remove obstructing membrane If available suction by means of a mechanical aspirating apparatus may be of great assistance a soft rubber catheter being inserted down the trachea through the tracheotomy wound Inspissated mucus in the trachea may tend to produce obstructive effects and cautious spraying with soda bicarbonate 15 grs to the ounce will help to loosen it whilst an expectorant mixture containing ammonium carbonate may also be pre scribed During fits of coughing a careful watch should be kept for displacement of the tube shown by return of dyspnœa stridor and recession of soft parts of the chest When the airway is well established and respiration comfortable the patient should be kept as quiet as possible for three or four days during which he is spoon fed On the third or fourth day plugging of the outlet of the tube with the finger or a rubber stopper may be tried for a few minutes to see if respiration may occur by way of the fenestra and the natural passages If the patient remains comfortable while this is being done the tube should be quickly removed and if there is no recurrence of dyspnœa for an hour or two after removal it is unlikely that re insertion will be required although in some cases this may

can be rapidly performed by the nurse seizing the string which usually lies on the post pharyngeal wall by means of dissecting forceps thus avoiding the more complicated operation of milking out the tube Some operators attach a silk string to the tube and bring it out of the mouth fixing it to the cheek with sticking plaster but the child soon learns to extubate itself by means of the tongue a most unsatisfactory manœuvre to both himself and the operator In successful cases the airway is at once re-established breathing becomes easy recession disappears colour and pulse improve and many patients are asleep in a few minutes The patient is returned to the steam tent for twenty four or forty eight hours and kept as quiet and undisturbed as possible a sedative such as Tinct Camph Co being given to soothe him and allay irritating cough If judiciously carried out spoon feeding is all that is necessary and we have yet to meet an intubated patient requiring to be fed by the nasal tube Medical aid must be available at a moment s notice for the tube may be blocked by membrane or be coughed out with the return of all the alarming signs of acute respiratory obstruction If the tube is not well tolerated and is repeatedly coughed out tracheotomy will have to be considered If this is decided on the intubation tube should be left *in situ* until the trachea has been incised and the tracheotomy tube about to be inserted the presence of the intubation tube in the trachea making the operation simpler Occasionally also intubation will fail to give the desired relief *e g* membrane may be rolled up in front of the tube or the tube may come to lie between a sheet of detached membrane and the tracheal wall In these cases recourse must be made to tracheotomy The great preponderance of cases however in which intubation fails are of the tracheo bronchial type and in these our experience has been that tracheotomy is no more likely to be successful than intubation From the moment of intubation the operator s mind should be fixed on extubation The tube is a foreign body in an acutely inflamed structure and in order to avoid ulceration and stenosis it is imperative that the tube should come out at the earliest possible moment Attempts therefore should be commenced on the third or not later than the fourth day We prefer to remove the tube in the morning so that the patient has the whole day to gain

this responsible duty The main disadvantage and of course a most serious one is that many have found that stenosis is unduly frequent after the operation This has not been our experience and we are inclined to believe that much can be done to avoid this sequel by extubation at the earliest possible moment

The apparatus we have employed in the past is the O Dwyer type with a vulcanite tube various sizes of tubes with their obturators being provided for various ages Prior to operation and following the practice of Ker there is threaded through the eyelet on the proximal end of the tube a banjo string from the terminal portion of which the metal covering of the silk core has been unwound The silk portion is knotted above and below the eyelet Indications for operation are exactly as for tracheotomy in hospital practice and when operation has been decided upon the patient is tightly wrapped up in a blanket so that the limbs are controlled He remains in bed all pillows are removed and he lies flat on his back near the right hand side The head is firmly held at the head of the bed so that the median plane is at right angles to the floor body movements being controlled by assistants The mouth is held open with a gag and the operator approaches the patient s right hand side The left forefinger is placed in the back of the throat and the operator feels for the epiglottis and the upper aperture of the larynx Keeping the introducer and tube strictly in the median plane with the right hand the tip of the tube is passed over the root of the tongue into the larynx being guided into that position along the palmar aspect of the left forefinger When the tip of the tube has engaged in the larynx the left forefinger is now moved to the proximal end of the tube and gentle pressure exerted to push it home At the same time the introducer is disengaged from the tube and before withdrawing the left forefinger the opening of the larynx should be explored to make sure the tube is *in situ* Actually the characteristic sound made by the patient breathing through the tube enables the experienced operator to know at once when it is properly in place The final step in the operation is to cut the semi rigid banjo string about the level of the posterior border of the soft palate the advantage of this being that in case of emergency blocking of the tube extubation



FIG ? X ay print of ntub t on tube *n* *l* Note banjo string pas ing up to pha ynx

[*T f p* 1]

confidence in himself obstructive signs having a tendency to recur during the night hours The patient should be carefully prepared by the administration of a hypnotic half an hour beforehand and the actual duty of removing the tube left to an experienced nurse who has the patient s confidence Quietly and with a complete absence of fu s the tube is removed by grasping with forceps the end of the banjo string presenting in the pharynx Every effort should be made to divert the patient s attention and should respiration remain normal for an hour or two further replacement is hardly likely to be necessary If obstructive signs return then re intubation is necessary The tube may be left in for another twenty four or forty-eight hours but a further attempt must be made to remove it at the end of this time and if this is also unsuccessful repeated efforts at extubation must be made at not more than forty eight hour intervals until the patient s respiration is satisfactory If the patient is unable to dispense with his tube in less than two weeks or as some insist within one week then tracheotomy should be performed A good deal of emphasis has been placed here on the necessity for early extubation and the procedure to be followed when delay in securing this is encountered but it should be remembered that in actual practice one reintubation is about the most that is ever required and patients who require repeated intubation are few Retained tubes are occasionally due to false passages or damage done to the larynx by too forcible methods in intubating Commonly they result from stenosis following ulceration due to pressure and Jackson recognises supra glottic and subglottic types of this The former he states may sometimes be cured by substituting a properly shaped and fitting tube, but it may require tracheotomy and the galvano cautery as will the subglottic type There is also a proportion of cases in which the difficulty of removing the tube is mainly psychological and much can be done by careful and tactful nursing to teach the patient to rely on his own airway

Direct Laryngoscopy We are strongly of the opinion that this should be routine procedure in the diagnosis and treatment of laryngeal diphtheria in hospital practice For details of the method the text books of laryngoscopy should be consulted We would mention however that the patient having been

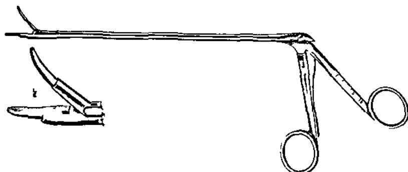


Fig. 8 Intubation forceps devised by the author for Direct Intubation through the laryngoscope

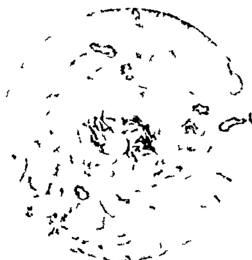


Fig. 9 Section of tonsil of convalescent carrier of C. diphtheriæ. Note cross section of crypt festooned with diphtheria bacilli.

pathological abnormalities and the general condition toned up with nourishing food and exercise in the fresh air Insufflations of dimol snuff directed into the nose and throat by an atomiser are helpful and if the patient will co operate douching with a solution of equal parts of sodium bicarbonate sodium biborate and sodium chloride 2 drachms to the pint should be carried out three or four times daily using ½ pint at each douching as recommended by Thomson Mann and Marriner (1930) Others have recommended spraying the throat and nose with a 1 in 500 watery solution of brilliant green with an atomiser delivering a fairly coarse spray Since the introduction of penicillin it has been employed in attempts to clear up carriers by means of lozenges throat sprays and nasal instillations containing the substance Success has been claimed for the method (Berman and Spitz 1945) and though it is worth a trial our own results so far have been inconclusive Should these measures fail after three or four weeks conscientious trial the nasopharynx should be thoroughly examined by a throat specialist with a view to operative treatment In throat carriers tonsillectomy can be relied on to terminate the carrier state in practically every case Nasal carriers should be examined with a view to clearing up such defects as hypertrophied adenoids Ear cases in which the diphtheria bacillus is usually associated with a chronic otitis media should also have the nasopharynx looked to and occasionally a mastoid operation will be necessary Proof of the termination of the carrier state should only be accepted when the patient has been given three consecutive negative cultures at weekly intervals

is exposed by the laryngoscope and the same type of intubation tube which is employed in the indirect method is introduced on a special introducing forceps In performing this operation in children we prefer to employ an adult size laryngo cope shortened to the length of the ordinary child s instrument A banjo string is attached to the cannula as before and when the latter is in position the wire is cut through after removal of the laryngoscope The after care of the patient and removal of the tube are as in the case of the indirect operation Once the technique of direct laryngoscopy is acquired direct intuba tion is a relatively easy operation to perform The fact that it is now possible to insert the intubation tube by sight removes several of the disadvantages of the original indirect method and in our practice since 1929 we have used the method with considerable success the indirect method having practically been abandoned

Treatment of Carriers Convalescent and persistent contact carriers should not be so designated unless the organism found on culture has been proved to be virulent The work of Thomson and McCartney and their co workers (1925) has shown that in almost every convalescent carrier some patho logical or anatomical abnormality of the nasopharynx is present and they have suggested that the organism leads a saprophytic existence in the inflammatory products resulting from these As far as the persistent convalescent carrier met with in hospital practice is concerned however the additional factor of re infection requires to be taken into account Employing the method of differentiation of diphtheria bacilli into gravis intermedius and mitis strains Glass and Wright (1938) have shown that the convalescent carrier accommodated in the multiple bed ward may show the presence in the upper respiratory tract of strains other than that concerned in producing his original illness From that they assume that in many cases the convalescent carrier state is brought about by reinfection The first step therefore in the treatment of the hospital convalescent carrier should be isolation in a single bed ward and Harries (1939) reports that this measure alone will often prove successful In patients however in which re infection cannot be held accountable for the persistence of infection efforts must be directed to the eradication of

pneumonia at autopsy During life the *blood picture* in whooping cough is characteristic A leucocytosis with a relative lymphocytosis appears at an early stage in the disease and is best marked at the third or fourth weeks at which times an average white count of 30 000 may be expected and a lymphocytosis of 60 per cent or over

Etiology Geographically whooping cough has a universal distribution but is most prevalent in cold and temperate climates and in the United Kingdom exhibits a definite seasonal prevalence from December to April In large urban communities epidemics show a tendency to recur every two to four years and Stocks (1932) from a study of whooping cough in Greenwich and Battersea in which outbreaks appear every second year has suggested that the periodicity of epidemics and their cessation may be attributable to a process of temporary latent immunisation occurring in contacts and lasting one year The incidence is greatest in children under five years but no age is immune and whilst the disease may be seen in infants a few weeks old Hall (1933) has pointed out that typical cases may occur at the other extreme of life At the present time whooping cough is of the highest importance as a killing disease and although as in other acute infections there has been a progressive fall in the death rate so that according to Bradford Hill (1933) in the decade 1921–30 it was one third of that in 1861–70 nevertheless in England and Wales in the former period it accounted for 44 000 deaths This number was slightly higher than that for measles and greater than the deaths from scarlet fever and diphtheria combined Ninety per cent of the deaths occur in the first five years of life the first two years showing the heaviest incidence of fatal cases Bradford Hill has drawn attention to certain peculiarities of whooping cough mortality For example it is greater in females than in males by 20 to 25 per cent at ages below five years it is less in illegitimate than legitimate children whilst he has also found that the less the overcrowding the earlier is the liability to attack and death

Transmission The source of infection is a case of the disease *but it is a relatively common experience in hospital* practice to find a case or cases appearing in a ward for which a source of infection in the shape of a definite case cannot be

CHAPTER V

WHOOPING COUGH

Synonym—Pertussis

Pathology Whilst the hypothesis that whooping cough may be a virus disease has been resuscitated by Rich (1932) experimental work such as that of the Macdonalds (1933) who have reproduced the disease by instilling living cultures of Haem pertussis into the nasopharynxes of susceptible children points to that organism originally described by Bordet and Gengou (1906) as the causal agent It is found in the sputum and can be isolated from droplets expelled during coughing on plates containing the appropriate medium this process being possible in a sufficiently large proportion of cases as to be recommended as a method of diagnosis by Madsen (1924) and others including Gardner and Leslie (1930) in this country The disease may be regarded as an upper respiratory tract infection with the usual signs of a catarrhal reaction in that region but in addition it has been suggested that an endotoxin acting on some part of the nervous system connected with the respiratory function is responsible for the paroxysmal attacks of coughing *Complement deviating antibodies* for Hæm pertussis according to Donald (1938) are found in the serum of those suffering from the disease with great regularity from the third week onwards reaching their maximum in the seventh or eighth weeks (Fig 30) Immunity reactions produced by the interdermal injection of killed cultures of Hæm pertussis have been described by a number of workers including Paterson Bailey and Waller (1935) but the specificity of these skin tests is now largely discredited No *characteristic post mortem changes are found in* fatal cases which have been uncomplicated the principal morbid changes being those of the broncho pneumonia to which death is usually due These are generally ascribed to secondarily invading streptococci or pneumococci but on several occasions in our own experience *pure cultures of Hæm pertussis* have been obtained from the lesions of whooping cough broncho

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Transmission The source of infection is a case of the disease but it is a relatively common experience in hospital practice to find a case or cases appearing in a ward for which a source of infection in the shape of a definite case cannot be

brought to light This suggests the possibility of a carrier state Kristensen (1933) however rejects this possibility as he was unable to demonstrate the carrier state in normal persons or in contacts and this view is also taken by Wilcox (1934) and Silverthorne (1935) Methods of bacteriological diagnosis however occasionally disclose abortive and exceptionally mild forms of the disease and it is to these that otherwise inexplicable outbreaks must be ascribed Infection is of the droplet type and it is doubtful if it is disseminated in any other way although F H Thomson (1916) could not exclude the occasional possibility of air borne infection beyond the usual limits of droplet infection as in chickenpox

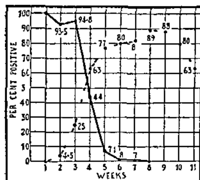


Fig 30 Graph according to A B Donald to show weekly incidence of positive cough plates (continuous line) and positive complement fixation tests (broken line) according to the stage of the disease in whooping cough

Infectivity The disease is less infectious than chicken pox or measles although Kelly and Reite (1934) have found the secondary attack in family susceptibles as high as 40 9 per cent which approaches their figure of 50 9 per cent for measles It is clear therefore that when opportunity for frequent and intimate contact occurs infectivity must be regarded as of a high order At the same time it should be realised that whooping cough infection is more amenable to control than measles or chickenpox and we have been able quite successfully to nurse cases of whooping cough at their most infectious stages in a barrier ward without transfer of infection a procedure which is quite impossible in the case of measles or chickenpox The disease is most infectious in the catarrhal stage becoming gradually less so in the paroxysmal and while Kristensen (1933) has been able to isolate the organism from a small percentage of cases from the fourth to the eighth weeks of the paroxysmal stage he believes that a period of isolation of four weeks from the commencement of the paroxysmal stage is sufficient As a result of their work at the North Western

Hospital both Westwater (1937) and Donald (1938) came to the same general conclusion and in view of the occasional persistence of the organism beyond the four week period suggested by Kristensen it might be logical to require two consecutive cough plates from patients before release

Incubation and Quarantine Periods Owing to the gradual onset of the disease the incubation period is difficult to assess but it is usually given as from 4 to 14 days A quarantine period of 21 days would give an ample margin of safety in susceptible contacts

Clinical Features Stage of Invasion This is usually known as the *catarrhal* stage and lasts from a few days to a fortnight It is very gradual in onset attention being drawn to the child by slight coryza and general malaise Some slight flickering of the temperature may also be present and a harsh spasmodic cough appears during the night This gradually becomes more frequent and distressing and finally the clinical diagnosis is disclosed by the occurrence of the typical whoop The catarrhal stage may occasionally be marked by the onset of a definite laryngitis which in a few cases is of such severity as to suggest diphtheritic croup with respiratory obstruction

Paroxysmal Stage This commences when the whoop appears at the end of a spasm of coughing The paroxysm leading to the whoop consists of a series of sharp explosive barks at the end of which there is a prolonged and somewhat violent stridorous inspiration During the spasm of which the patient may have had no warning he leans forward with congested face terrified expression eyes almost protruding When the whoop comes a certain amount of relief is obtained and the child expectorates sticky mucus mixed with the vomit which is invariably the concluding act of the spasm Frequently also during the paroxysm control of the sphincters is lost After the spasm the child sinks back exhausted but if it has been severe it may end in a convulsion Paroxysms vary greatly in number according to the severity of the attack and may be as few as five or six daily or as many as twenty or thirty They tend to be more frequent at night and though often spontaneous the spectacle of another child in a spasm will sometimes set them off whilst throat examination or the

taking of food or drink may also be a precipitating factor In intervals between spasms the child obtains sleep, may ask for food and play with his toys The facies is characteristic pale puffy and dull and if vomiting is frequent he loses weight Pyrexia is usually absent and physical examination of the chest only reveals a few rales In the average case this stage lasts from four to eight weeks

Stage of Convalescence Paroxysms gradually diminish in intensity and the child ceases to vomit later to whoop and finally to cough *Pari passu* with this the expression becomes more alert and the general nutrition rapidly improves but it should be remembered that once having learnt to whoop a child may continue the habit for months afterwards especially in emotional crises as a means of attracting sympathy Catarrhal infection of the upper respiratory tract some weeks or months after recovery may also lead to temporary recrudescence of the whoop

Complications Some degree of *bronchitis* is present in the catarrhal and paroxysmal stages but of the complications of whooping cough *broncho pneumonia* is by far the most fatal When it occurs it begins at the height of the paroxysmal stage and in its clinical features conforms to the broncho pneumonia of childhood generally with elevated irregular temperature rapid grunting respirations rapid pulse and patchy consolidation with abundant crepitations Fortunately there is a diminution or disappearance of the more pronounced manifestations of the paroxysmal cough during this complication but a sufficient amount of this distressing feature may contribute to the general exhaustion of the patient The complication runs its course in from one to three weeks but if it lasts as long as the latter period death from heart failure or convulsions is not infrequent During the course of broncho pneumonia a careful watch for *empyema* should be kept If immediate recovery takes place much disability may follow in later childhood from *pulmonary fibrosis* As in measles an attack of whooping cough may terminate in tuberculous broncho pneumonia or acute miliary tuberculosis

Convulsions are also a serious and not unusual complication of whooping cough They may be set up by a paroxysm of coughing or occur independently and are specially prone to



Fig 31 Subconjunctival hæmorrhage in whooping cough almost complete in right eye and confined to upper half of conjunctiva on left Also note black eye on right



Fig 3 Fatal case of cancrum oris occurring as a complication in whooping cough

occur in cases complicated by broncho pneumonia or in undernourished ricketty children

Acute gastro enteritis occurring during the paroxysmal stage may also be a serious complication Frequent vomiting and diarrhœa lead to rapid wasting and since the patient s nutrition is already undermined fatal cases are by no means uncommon

Acute otitis media may also occur as a complication

Owing to the strain of coughing various *pressure* complications may be found *Epistaxis sub conjunctival hæmorrhages* and *black eye* are occasionally encountered and we have had one case under observation in which copious hæmorrhages occurred per vaginam and per rectum whilst numerous petechiæ formed in the skin Increased intra abdominal pressure may result in *hernia* chiefly at the umbilicus and *prolapse of the rectum* *Surgical emphysema* is sometimes seen *Ulcer of the frænum* of the tongue due to its protrusion during spasms with consequent pressure on the lower incisors is said to occur in about half the cases and may be of assistance in diagnosis

Ulcerative stomatitis is not uncommon but *cancrum oris* is now very rare

Whilst not infrequently found in association with measles whooping cough does not appear to have any particular association with other diseases Relapse and second attacks are practically unknown

Varieties of the Disease Whilst there is an infinite series of gradations in severity of whooping cough there are no specially severe types which may be differentiated by their manifestations or clinical course from the usual form of the disease *Abortive types* in which the disease runs a shortened course without the appearance of the typical whoop and with little constitutional disturbance are by no means uncommon Indeed bacteriological evidence would suggest that occasionally whooping cough may be denoted by nothing more than a simple bronchial catarrh lasting a few days Again and this is particularly the case in small infants the illness may be severe and the cough most harassing but the typical whoop is never developed even although during the spasms the child may go almost black in the face

Diagnosis A history of exposure and the presence of a

cough becoming progressively worse and tending to be spasmodic strongly suggest whooping cough in the catarrhal period but on clinical grounds alone in the absence of an epidemic or a history of exposure it is difficult to see how a diagnosis can be made at this stage There is no doubt that valuable support is given to the diagnosis if a well marked lymphocytosis is obtained on blood examination and in hospital practice we have found this method of much assistance Once the whoop is established the diagnosis is simple The characteristic facies and the frenal ulcer may help when a typical spasm is not observed but the latter will usually be elicited when the throat is examined In abortive cases the diagnosis will not be made with certainty unless definite contact with other cases can be established but here again blood examination will help In differential diagnosis simple bronchitis laryngismus stridulus and enlarged hilar glands causing an explosive cough may require consideration whilst the laryngitis of the catarrhal stage may simulate streptococcal laryngitis laryngeal diphtheria or measles laryngitis

Bacteriological Diagnosis For the protection of other children it is essential to isolate the patient at the earliest possible moment in the catarrhal stage and to this end it is to be hoped that progress will be made with the cough plate method which it is claimed will make the routine bacteriological diagnosis of whooping cough as simple as in diphtheria Madsen (1924) and Gardner and Leslie (1932) have been able in this way to isolate *Hæm pertussis* in 75 per cent of their cases in the catarrhal stage whilst Sauer (1932) and Silverthorne (1935) have reported successes in practically every case From the results obtained by Westwater (1937) and Donald (1938) under our own observation at the North Western Hospital we are convinced that the method shows a high degree of reliability and can be readily carried out after some experience by those with no highly specialised bacteriological training For details of the special potato glycerine blood agar medium the current bacteriological literature must be consulted but in our own practice that containing 50 per cent citrated horse blood has given most consistent results It should be freshly made and poured into petri plates These are exposed at a distance of 3 or 4 inches from the mouth to

two or three natural spasms of coughing and sent to the laboratory as soon as possible Typical colonies do not appear until the lapse of two to four days a positive report indicating the presence of whooping cough The complement fixation test is not of much practical importance in diagnosis but it might be carried out where it is important to establish the diagnosis in cases which had already lasted for six to eight weeks

Prognosis This depends largely on the age and general nutrition of the patient Children under two years and particularly those under one are specially vulnerable whilst the outlook for rickety and malnourished subjects is poor The severity of uncomplicated cases stands in direct relationship to the frequency of paroxysms and to the ability of the patient to maintain weight and obtain rest In broncho pneumonia the outlook is grave fatality rates of 25 to 50 per cent occurring in patients with this complication The onset of convulsions is also ominous and while a child may suffer from one or two during an attack and be little the worse their appearance must be regarded with concern as they tend to recur more and more frequently until before death they become continuous Gastro enteritis is also serious and when as sometimes occurs this is superimposed on broncho pneumonia the outlook is very bad Other complications usually respond to treatment and require no special commentary

Prophylaxis For the same reasons which have been advanced in the case of measles all cases of whooping cough occurring in England and Wales have been made notifiable by regulations issued by the Ministry of Health (1939) and also as in the case of measles these supersede any local regulations which may have been in force although the latter do not seem to have been employed by local authorities to the same extent as in measles General measures include isolation of the patient and bearing in mind that effective isolation is of considerable practical value in preventing the transfer of infection in whooping cough and also that if it is to be successful it should be carried out at the earliest possible moment every effort should be made to make it prompt This in turn depends on early diagnosis and considering the success obtained from the cough plate method in this and other countries more use of it might be made by public health departments than is the

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with convalescent whooping cough serum has given promising results in the hands of Meader (1937)

Treatment So far no specific remedy for whooping cough has appeared Much work has been done with vaccines but we agree with the majority that they are of doubtful efficacy The results obtained from the use of convalescent whooping cough serum are also somewhat unconvincing and the first essential in treatment therefore is to isolate the patient in as hygienic circumstances as possible and maintain these during the illness In the catarrhal stage the patient should be put to bed in a well ventilated room and at all times some responsible person should be at hand to comfort and support him during spasms He should be warmly clad and a firm abdominal binder applied If later on the patient remains afebrile and uncomplicated and spasms are infrequent the patient may do quite well out of bed especially if he can be taken to the open air without coming into contact with others When spasms are frequent however he should remain in bed and be encouraged to rest as much as possible between paroxysms In appropriate weather the bed should be wheeled out of doors and provided proper arrangements are made to protect from bitter winds an open air régime is the ideal In London there were not a great many days when our patients could not be wheeled out on the ward balconies and even in the sterner climatic conditions of Edinburgh open air treatment has been traditional since its inception by Ker Feeding is also of first class importance frequent small feeds being indicated and if one feed is lost as the result of a spasm another should be given once the patient has settled down again Infants will require a milk diet appropriate for their age and this may be peptonised or citrated to facilitate digestion Older children should be given an abundant mixed diet while some special delicacy will occasionally tempt those with poor appetites Cod liver oil and malt or virol may be used to supplement the diet In severe cases when wasting occurs rectal salines containing 10 per cent glucose may be tried but we have not found these always successful as coughing may interfere with retention Intravenous salines containing 5 per cent glucose are more useful but if the patient s condition makes their administration impossible reliance will require to be

case at present Contacts are excluded from school for twenty one days For a number of years many local authorities have made provision in their infectious hospitals for the treatment of whooping cough cases being specially selected on the grounds of complications or poor home conditions This is supplemented by assistance in home nursing and in a few cases by the provision of periods of convalescence in the country after the termination of the illness

Specific prophylaxis Many workers have attempted to estimate the efficiency of the injection of killed cultures of Hæm pertussis in producing active immunity against whooping cough Probably the best known field work is that of Madsen (1933) who made two large series of observations during epidemics in the Faroe Islands in 1923–24 and 1929 In the latter success was claimed both in prevention of the disease and in reducing mortality but to get good results Madsen emphasises that the vaccine should be made from young strains the dosage should be large—a total of 22 000 million organisms and that inoculation should be completed shortly before the onset of the epidemic Sauer has also done a considerable amount of work on whooping cough prophylaxis and recommends (1937) three subcutaneous injections at weekly intervals of a vaccine containing 10 billion organisms per cc, a total dosage of 8 cc being given for those of two years and under and 10 cc to those above two years inoculation being commenced between six and twelve months of age to allow for an adequate period between inoculation and possible exposure Some well controlled observations have been published by Kendrick and Elderling (1939) whose data also suggest that a definite active immunity follows injection of whooping cough vaccine Other workers *e g* Siegel (1939) are more sceptical and in an experiment in England McFarlan Topley and Fisher (1945) were unable to find support for the view that pertussis vaccine is of value in the prophylaxis of whooping cough Our present view is that as a result of the advances in knowledge of the antigenic properties of Hæm pertussis made by Gardner and Leslie (1391) the position is probably more encouraging than hitherto but in the meantime it would be wise to regard specific prophylaxis in whooping cough as still in the experimental stage Passive immunisation

placed on daily subcutaneous or intraperitoneal salines in 80–100 cc amounts for a few days Innumerable drugs have the reputation of alleviating the paroxysms of whooping cough but their very number indicates their doubtful efficacy We have tried belladonna antipyrin benzyl benzoate ephedrine and intramuscular injections of ether among others but in the end have usually come back to belladonna reported by Ker to be as useful as any in controlling spasms To be effective it must be pushed in 2 to 8 or 10 minim doses four hourly careful watch being kept for a few days In more severe cases we agree with Benson (1935) that luminal in $\frac{1}{8}$ grn to $\frac{1}{4}$ grn doses three times daily occasionally results in rapid amelioration of symptoms but in view of its toxicity discretion in its use is indicated After systematic trial we cannot support the conclusions of those who have found improvement to follow ultra violet radiation and indeed we have thought occasionally that this treatment has stirred up chest complications which might otherwise have remained quiescent Benefit has also been claimed from exposure to X rays but the evidence as to the results is conflicting *Broncho pneumonia* should be treated on open air principles frequent nourishing feeds poultices and hypodermic stimulation by strychnine or coramine One of the sulphonamides should be administered but our experience has been that in whooping cough pneumonia the results are most disappointing and these drugs have had nothing like the success which has followed their use in the corresponding complication of measles In whooping cough pneumonia the use of the oxygen tent has yielded good results and on occasion has proved almost specific in its action Should empyema occur repeated aspiration may be sufficient but a few cases will require drainage Convulsions are treated by the mustard bath and luminal or chloral and bromide In severe convulsive states we have found a lumbar puncture disappointing but temporary relief may be obtained by light general anaesthesia and we have been favourably impressed recently by the administration of subcutaneous or intraperitoneal injections of 50–200 c c of saline in these cases In gastro enteritis frequent small feeds of whey and glucose should be given and the bowel irrigated with warm saline or eusol once daily Washing out the stomach with

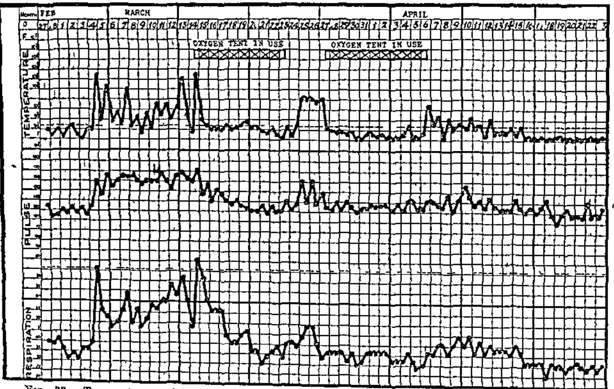


FIG 33 Temperature pulse and respiration chart of male aged sixteen months suffering from whooping cough broncho pneumonia Note the improvement in the condition as shown by these records on two occasions following the use of the oxygen tent and the intervening relapse when the tent was discontinued

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saline and then leaving a feed in the stomach is also a useful measure

Period of Isolation Bacteriological work at the North Western Hospital supports the clinical observation that infectivity after the fourth and certainly after the sixth week is negligible and this fact is of particular importance in the matter of duration of the period of isolation One of the main administrative difficulties encountered in connection with the hospital treatment of whooping cough is the prolonged period required if patients are to be detained until the cough has ceased We are of the opinion that this is necessary in only a few cases, since by the end of a month the more serious possibilities of the disease are unlikely to present themselves and with ordinary attention the patient s progress is likely to be uninterrupted The public require to be educated in this so that suitable cases may be discharged from hospital though cough is still present Use also might be made of cough plates to determine cessation of infectivity two consecutive negative plates being accepted as evidence of this With such a safe guard many patients could be released from hospital much earlier than has commonly been the practice and valuable beds made available for those in the earlier and more dangerous period of the disease The same arguments apply in respect of the period of school exclusion which at present as recommended by the Ministry of Health and the Board of Education is six weeks We agree with Gardner (1936) that this could be shortened in many cases by the adoption of a bacteriological standard of freedom from infectivity with consequent saving of school time

CHAPTER VI

CEREBRO-SPINAL FEVER

Synonym—Cerebro spinal meningitis Spotted fever

Pathology The causal organism is the meningococcus which by appropriate staining methods may be demonstrated in the cerebrospinal fluid naso pharyngeal and conjunctival secretions and in the blood of cases of the disease It can also be isolated from the nasopharynx of contacts and carriers From the epidemiological point of view it should be recognised that there are important serological differences within the group of organisms defined by the term meningococcus Scott has classified these on a basis of agglutinability into two main groups I and II Group I comprising the types 1 and 3 and Group II the types 2 and 4 differentiated earlier by Gordon but it should be understood that the antigenic relationship between individual strains in a given group or type may be relatively remote The organism gains entrance into the nasopharynx and some take the view that extension to the meninges is by way of the olfactory nerve sheaths whilst others such as Embleton (1910) believe that the organism may pass through the bony wall of the sphenoidal sinus At present however it is generally accepted that invasion takes place by way of the blood stream and E G D Murray (1929) summarised this conception by defining the pathological process in cerebro spinal fever as in reality a pharyngitis with occasionally a generalisation in the form of a septicæmia which in turn is usually complicated by localisation in the meninges and occasionally in the skin and much more rarely in serous cavities joints endocardium and other sites On the whole this has been accepted as fitting in with clinical experience since while in some cases the condition remains limited to a septicæmia in the great majority and especially in severe cases associated with a rash although epticæmia may occur in the early stages the meningococcus in almost the first stages shows a selective affinity for the sub arachnoid space Recently however Banks and McCartney (1942) have produced evidence

that meningococcal infection of the central nervous system is not limited to meningitis careful histological examination of the brain and cord showing the presence of encephalitis acute encephalomyelitis or meningitis with focal encephalo myelitis Several of the clinical features of the disease are suggestive of a toxic action Ferry (1931) described a soluble exotoxin but although some clinicians have reported favour ably on his antitoxic serum this work did not gain general acceptance among laboratory workers and toxic effects are generally ascribed to the endotoxin described by Gordon who emphasised its importance as an antigen in the production of therapeutic sera The typical lesions seen post mortem are acute inflammatory changes in the arachnoid with purulent effusion into the sub arachnoid space Purulent exudate is found over the base cerebellum and pons and also in some cases over the vertex The spinal membranes and cord show similar changes whilst pus may be found occasionally in joints If death has occurred after the illness has lasted for two or three weeks distension of the ventricles with thinning of the brain substance and flattening of the convolutions is usually found In encephalitic lesions intense congestion and œdema small hæmorrhages and capillary thrombosis are found in the rapidly fatal cases whilst in less acute forms perivascular cuffing is found in addition according to Banks and McCartney Adrenal hæmorrhages are also found in certain of the fulminating types

Etiology Cerebro spinal fever has a general distribution throughout the world occurring in both temperate and tropical climates with no special racial susceptibility In the United Kingdom since the beginning of the twentieth century there appear to have been four phases of epidemic prevalence in 1907 in the war years 1915–19 in 1931 and again in 1940 The maximum incidence is in the late winter and spring months excessive humidity or sharp spells of cold weather being frequently followed by increased incidence Males are more often attacked than females After middle life cases are uncommon and generally speaking the chief prevalence is in children under five years although as a special report of the Ministry of Health (1931) points out outbreaks in older children and young adults in special communities such as

schools or military camps tend to obscure this when the age incidence is calculated in limited administrative areas As an example of this 12 per cent of the patients admitted to the Edinburgh City Hospital in the 1940–41 epidemic were aged forty years and over While case fatality rates vary as between one epidemic and another in the past they have been invariably high from just under 40 to over 80 per cent They were most favourable at the five to twenty age period and least favourable under one year of age whilst in those over forty years they did not fall far short of those occurring in infancy With the introduction of chemotherapy however our views on this aspect of meningococcal meningitis have required material revision as will be seen from a study of the table of the com parative results of serum treatment and chemotherapy on a subsequent page A total case fatality of under 20 per cent at all ages was found and whilst the age groups at the extremes of life still show the highest case fatality rates those in the early years are much reduced and the five to twenty age group formerly the most favourable is now so favourable that fatal results are uncommon From his studies during the 1914–18 war Glover (1918) showed that by far the most important pre disposing factor in producing epidemic prevalence was over crowding especially in ill ventilated sleeping quarters This causes a rise in the meningococcal carrier rate in some cases from 20 to 60 per cent and when this reached 20 per cent cases were likely to appear Later investigations however by Dudley and Brennan (1934) indicate that there is no constant correlation between high carrier rates and the occurrence of cases the latter depending in their opinion on the virulence of the prevailing epidemic strain Other predisposing factors generally recognised are physical and mental stress

Transmission The source of clinical infection is almost invariably a carrier E G D Murray reporting that 95 per cent of cases arise in this way and not from previous cases This agrees with our own experience as we have rarely observed instances of familial infection Transmission is by droplet infection or direct contact with nasal conjunctival or oral *discharges and since the* meningococcus only supports existence away from the human host with difficulty an intimate degree

that meningococcal infection of the central nervous system is not limited to meningitis careful histological examination of the brain and cord showing the presence of encephalitis acute encephalomyelitis or meningitis with focal encephalo myelitis Several of the clinical features of the disease are suggestive of a toxic action Ferry (1931) described a soluble exotoxin but although some clinicians have reported favour ably on his antitoxic serum this work did not gain general acceptance among laboratory workers and toxic effects are generally ascribed to the endotoxin described by Gordon who emphasised its importance as an antigen in the production of therapeutic sera The typical lesions seen post mortem are acute inflammatory changes in the arachnoid with purulent effusion into the sub arachnoid space Purulent exudate is found over the base cerebellum and pons and also in some cases over the vertex The spinal membranes and cord show similar changes whilst pus may be found occasionally in joints If death has occurred after the illness has lasted for two or three weeks distension of the ventricles with thinning of the brain substance and flattening of the convolutions is usually found In encephalitic lesions intense congestion and œdema small hæmorrhages and capillary thrombosis are found in the rapidly fatal cases whilst in less acute forms perivascular cuffing is found in addition according to Banks and McCartney Adrenal hæmorrhages are also found in certain of the fulminating types

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of contact is necessary to establish infection The organism obtains entrance into the nasopharynx by inhalation

Infectivity In closed communities under favourable circumstances carrier infection may become widespread in a relatively short time but if we only include clinical cases as evidence of infection the disease is of low grade infectivity and actually it is often nursed in the wards of general hospitals without the occurrence of other cases whilst infection among medical and nursing staffs of infectious hospitals is practically unknown The power of infecting others must be assumed from the moment of receiving the infecting dose of organisms and certainly *from the appearance of the first* symptom but in the great majority of cases infectivity will have disappeared before the patient s general condition permits return to his usual surroundings If desired however West s nasopharyngeal swabs may be employed for making cultures for the determination of infectivity by bacteriological methods in convalescents and carriers These should be passed behind the soft palate and pressed firmly over the post pharyngeal wall and brought into contact with the adenoid pad Two or three consecutive swabs negative for the presence of the meningococcus will be necessary before regarding the individual as free from infection

Incubation and Quarantine Period The incubation period is usually short from two to four days but periods as short as twenty four hours and as long as ten days have been reported Quarantine is not imposed on contacts except in school children and in certain circumstances such as in military camps

Clinical Features In the bulk of cases the onset of symptoms is sudden Some degree of nasal and conjunctival *catarrh* is often present and the former may become profuse as the disease advances The chief complaint is of intense *headache photophobia stiffness of the neck* and possibly stiffness and pain referred to the spine *Vomiting* often projectile in character occurs early and is a constant sign there may be *rigors* and in children *convulsions* Pyrexia is present usually from 102 to 104° F but is very variable and although in general a relatively slow pulse is encountered at the outset it may be rapid and soft As a rule when first seen the patient is flushed restless and apprehensive In many cases indeed he will be

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FIG 34 Hæmorrh ıg c ra h of cerebro spınal fe\ er ın adult female] atient Although slightly more profu e than usual the ra h may be regarded as typic ıl consisting mainl) of petechiae se\ eral larger spots and sł owing one purpuric smudge ın the skın of the epıgastrıum

[T fac p 133

found throwing himself about in bed shouting and moaning having become utterly distracted by the excruciating headache When he comes to rest it is usually in the prone position with head bent back and face half turned to the pillow Infants usually lie on the side with head retracted and back arched in the gun hammer position Although resentful of handling irritable and confused the patient may be able to answer questions but if he realises his visitor is his medical attendant his only concern will be to ask for something to put away his headache Even at this early stage in a few cases *deafness* will be present Extreme degrees of *delirium* in adult males are not uncommon when it will require the undivided attentions of several attendants to keep the patient in bed Again in a certain proportion of cases the patient passes into *coma* within a few hours of onset On examination nuchal rigidity is readily made out bending the head forward being very painful the patient raising head neck and shoulders in one piece but in infants this sign may not be elicited until the movement is repeated several times Kernig s sign is usually well marked although its appearance may be delayed for a day or two and in infants it may be absent Brudzinski s sign is also frequently present but apart from the absence of abdominal reflexes attempts to elicit tendon reflexes give varying responses *Rashes* have given the disease its colloquial name of spotted fever and are common in some outbreaks During the 1940–41 epidemic in Edinburgh they were present in 40 per cent of cases but in the general run of sporadic cases seen over a number of years they have not been a conspicuous feature Commencing as small erythematous macules scattered irregularly over the body and limbs in a matter of hours they become petechial spots dark red or purple in colour occasionally grouping themselves in clusters about the size of finger nail The great majority of rashes conform to this type but occasionally large purpuric blotches appear early in the very severe cases From the fourth to the seventh day of onset *herpes* with a zoster distribution on the lips forehead and cheeks external ears trunk and limbs is frequently seen in a recent series of cases in almost exactly 20 per cent and this may add appreciably to the discomfort of the patient The progress of the disease depends on the response to chemo-

therapy Cases which do not respond remain irritable in a restless stupor Spasms of pain are frequent retching and vomiting continue the stomach contents often being of the coffee ground type Double incontinence is frequent the patient becomes comatose the respirations quicken the pulse is running and irregular and death is often preceded by a rise in temperature sometimes to hyperpyretic levels In fatal cases which have received drug treatment over 75 per cent of the deaths have taken place in the first week The favourable case shows a marked improvement in three or four days sometimes even within twenty four or forty eight hours While perhaps a little confused irritable or emotional head ache diminishes vomiting ceases pain in the neck and back disappears although various aches and pains persist for a few days longer neck rigidity abates and appetite is relatively quickly regained In practically all cases whether recovery ensues or not the temperature comes down to normal levels within a day or two and in successful cases these are main tained At the end of two or three weeks the patient will be able to get up and all but a few will be able to resume a normal existence in from four to eight weeks from the onset of illness Intermediate between the acute fatal cases and those which recover a certain proportion progress to a *chronic stage* which may be prolonged for several weeks These cases seem to have been commoner in the early days of serum treatment when access to the spinal canal was limited to that obtainable by lumbar puncture Later when drainage by cisternal and ven tricular puncture became possible they appeared relatively infrequently and since the introduction of chemotherapy we have only seen one or two cases in which a minor degree of this condition might be said to have been present The signs are due to increase in intraventricular pressure resulting from block in the cerebrospinal circulation which may be revealed during lumbar puncture by the absence of Queckenstedt s sign The characteristic clinical features are *progressive wasting* to an extreme degree persistence of Kernig s sign and neck rigidity head retraction and greater or less degrees of opis thotonos this being very marked in young children *Frequent* vomiting spasms of the limbs and convulsions occur whilst squint nystagmus ptosis and exopthalmos are not infrequent

Blindness and deafness and in infants marked bulging of the fontanelles or even in some cases separation of the cranial bones at the sutures result from tension in the ventricles With rare exceptions the patient passes into coma and death

Complications In the past our experience derived mainly from serum treated cases of the sporadic type was that while the case fatality was high complications were not very common and the same may be said regarding the incidence of com plications in patients treated by chemotherapy Apart from herpes which is so common as to be regarded almost as a part of the disease the most frequent complication in our

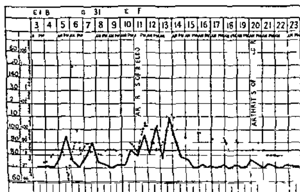


Fig 35 Temperature and pulse chart of case of cerebro spinal fever treated by sulphapyridine and showing arthritis as a complication

cases recovered after sulphapyridine treatment has been *arthritis* which occurred in 4 2 per cent of all cases Over one third of the patients were in the twenty to thirty age group and it seemed to be slightly commoner in males the condition usually appearing in the second week of the disease Usually single joints were involved but multiple joint lesions were not unusual and arthritis was often accompanied by myositis and tenosynovitis In the order of frequency of involvement were the elbow shoulder knee and ankle *Neuro labyrinthitis* resulting in nerve deafness was next commonest and occurred in 2 per cent of the cases This is a distressing complication marked as often as not by complete and permanent deafness although the more fortunate may only develop a unilateral or

partial form One of our patients however who was discharged from hospital stone deaf spontaneously recovered in three months *Neuritis* in the upper or lower limbs occurred in 1 8 per cent of sulphapyridine treated cases This may result in a prolonged period of disability and even permanent loss of function but in some cases a perceptible degree of recovery is obtained Incidentally we have seen patients suffering from this complication before they had been given sulphonamide Neuritic pain in the lumbar region and along the course of the sciatic nerve has also been noted but since this was also occasionally encountered in serum treated cases and cleared up in a week or two it is possibly traumatic in origin and results from lumbar puncture *Uveitis* an interesting complication of which we have seen only one example appeared in the first week of illness and cleared up rapidly as chemotherapy was continued leaving a normal eye with normal vision *Abortion* occurred in the only two pregnant women we have had the opportunity of treating with sulphapyridine but both made uncomplicated recoveries *Broncho pneumonia* is sometimes seen as a terminal complication in fatal cases as also is heart failure due to *toxic myocarditis* Such residual phenomena as *blindness* and *mental impairment* often reported in the past after recovery following serum treatment have not been observed but a few of our patients have shown *squint ptosis* or *facial paralysis* on discharge from hospital In a proportion of adults recovery seems to be marred by persistent headache often described as dullness worst in the morning and passing off during the day On occasion it has remained for months A War Office Memorandum (1942) has drawn attention to a group of *central nervous symptoms commonest in males between the ages of* fifteen and forty five which are stated to be among the most frequent sequelae of cerebro spinal fever They include headache giddiness minor mental and emotional disturbances *alteration in personality* insomnia and fatiguability a clinical picture closely resembling that following closed head injury Whilst those in civil practice are unlikely to have the facilities possessed by the military authorities for following up their cases the above syndrome *will be perfectly familiar to those who* have had much opportunity of studying the disease Whether

it is as common in civil life is not easy to determine but if it is it seems likely that more would have been heard of it and only less gratifying than the great saving of life effected by the introduction of chemotherapy is the complete restoration to normal of the great bulk of recovered cases *Conjunctivitis* occasionally progressing to *keratitis* and *corneal ulcer* and *acute otitis media* have been somewhat uncommon in our experience whilst of *orchitis* reported by others following chemotherapy we have not seen a single example

Relapse The frequency of this has been much discussed and although in our case records has not been frequent we have seen instances of recurrence of signs and symptoms after a period during which the cerebro spinal fluid has been perfectly clear sterile and all the signs of recovery evident After chemotherapy true relapse is very unusual appearing in less than 0 5 per cent of our patients although in a few cases the return of persistent headache when chemotherapy has been discontinued and which has promptly yielded to a further course of drug treatment suggests the possibility of intercurrent relapse

Varieties of the Disease Whilst the clinical course of the majority of cases will conform approximately to the above description in epidemics a *fulminating* form in which death occurs in twenty four hours or less has not been uncommon and is said to occur in two or three per cent of all cases In the past it was customary to ascribe the rapidly fatal issue to an overwhelming meningococcal septicæmia as whilst the cerebro spinal fluid is frequently clear the organism can readily be recovered from the blood The work of Banks and McCartney has thrown additional light on the pathogenesis of this condition two types of which are described a fulminating *adrenal* and a fulminating *cerebral* The former is characterised by sudden onset of fever rapid deterioration vomiting a generalised petechial rash with larger purpuric elements and the development of grave hypotension with cyanosis The mental condition is relatively clear but only when infection is restricted to septicæmia with adrenal hæmorrhage In the fulminating cerebral type the larger purpuric elements are absent from the rash whilst stupor and coma are prominent and early This is the type in which the characteristic morbid

histology is that of an *early encephalitis* The same authors describe a slightly less intense form than the fulminating an *acute encephalomyelitis* Clinically this is characterised by signs of an acute meningitis which rapidly becomes complicated by encephalitic signs especially sustained deep coma cyanosis and rapid or stertorous and irregular breathing These cases usually end fatally within a few days without regaining consciousness but recovery with transient Parkinsonism has been noted A third main cerebral syndrome is presented by Banks and McCartney as *meningitis with focal encephalitis* The clinical picture is then said to be diverse including protracted and recurrent delirium with sudden collapse or sudden convulsions with secondary coma and death or even deep coma resulting from large sub dural hæmorrhage Other varieties include the *septicæmic* form or meningococcæmia to which attention has recently been drawn although its occurrence usually in adults has always been well recognised by those with special experience in infectious disease It shows itself by a period of continuous temperature lasting for days or even weeks generalised pains and involvement of joints or serous cavities A rash resembling erythema nodosum may appear on the limbs or trunk and though some have suggested that this is characteristic of meningococcæmia it is well to rely on the results of blood culture for diagnosis since we have encountered similar eruptions in streptococcal septicæmia A feature of some cases has been striking remission of temperature followed by recrudescence and the appearance of further skin lesions Several cases seen in the past have yielded rapidly to the intravenous administration of antimeningococcal serum whilst more recently they have been treated by chemotherapy with excellent results As has been observed in the section on pathology the condition may be limited to a septicæmia but in cases which have remained undiagnosed—they are frequently mistaken for acute rheumatism—meningitis may supervene at as late a stage in the disease as the seventh week as reported by Dickson Magner McKinnon and McGillivray (1941) although the preliminary septicæmic stage does not commonly last longer than a week or two *Mild* or *abortive types* may be met with particularly towards the end of an epidemic In these there may be malaise headache general

aching pyrexia and some degree of Kernig s sign but in a few days the temperature becomes normal and recovery takes place When mild types of the disease occur in infants the true nature of the condition is apt to be overlooked and in the absence of diagnosis and treatment progress to a chronic localised form of the disease commonly termed *post basic meningitis* In this the purulent inflammatory exudate is mainly distributed over the base of the brain The clinical features resemble the chronic form which as it drags on shows all the signs of well marked internal hydrocephalus

The Cerebro spinal Fluid In cerebro spinal fever the fluid obtained on lumbar cisternal or ventricular puncture comes off under increased pressure the manometer reading quite frequently being over 300 mm In appearance it may vary from slightly hazy to purulent the cells being predominantly polymorphonuclear and the typical gram negative diplococci can generally be demonstrated by simple staining methods In the early stages and particularly if intra thecal serum has not been administered the fluid may be almost clear and this feature of the fulminating case has already been commented on On microscopic examination cells and organisms may be scanty and indeed prolonged search may fail to reveal the latter When found the majority are extracellular As the disease progresses cells and organisms become abundant and if recovery ensues the organisms become predominantly intra cellular swollen ghost forms are seen the fluid gradually becomes less turbid and under less pressure until it becomes crystal clear and under normal pressure Various alterations in the biochemical constituents are also found Glucose is very much diminished protein is increased and chlorides are reduced From the practical point of view the estimation of glucose is probably the most important since a simple and roughly quantitative test can be performed at the bedside We employ the method suggested by Ker in which 1 0 cc of Fehling s reagent diluted 1 in 4 is added to 10 cc of cerebro spinal fluid On boiling normal cerebro spinal fluid will show rapid and abundant reduction of the copper salt whereas in various forms of meningitis including the meningococcal variety reduction is absent or partial This test whilst valueless in diagnosis is of considerable aid in

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and neck being shaved Except possibly in infants a general anæsthetic is also necessary It should only be carried out by an experienced operator in whose hands it will sometimes give results otherwise unobtainable since it gives access to spaces shut off from drainage by adhesions above the lumbar region Whilst in the past during the administration of serum cisternal drainage became necessary owing to spinal block resulting in dry taps on lumbar puncture since the introduction of chemotherapy the procedure will only be required on the rarest occasions It should not be employed as a routine for as long as free flow of fluid is obtained on lumbar puncture there seems no particular reason for choosing a method in which the margin of safety is probably less To carry it out the patient s head is bent forward on the chest and an imaginary line mapped out between the glabella or a point slightly above it and the upper margin of the external auditory meatus Where this line cuts the mid line of the neck posteriorly is the point of insertion of the needle A specially stout short instrument graded in centimetres is used for the operation Its entrance into the skin as indicated above is just above the spinous process of the atlas and the direction which should be imparted to the needle is given by the line between the glabella and meatus In this way after gentle pushing it will impinge on the under surface of the occipital bone The point is then slightly depressed and the operator carefully feels his way along the occipital bone until the occipito atlantoid ligament is reached about 4 to 5 cm from the skin surface The last few millimetres should be cautiously traversed as the intention is to enter the cistern and no more for if the needle is too far advanced damage to the floor of the fourth ventricle with sudden cessation of respiration and death may follow If the signs of increased intraventricular tension are marked cisternal puncture may be dangerous since the cerebellum may be pushed down into the foramen magnum with resulting damage to the middle lobe when the occipito atlantoid ligament is pierced In such cases if cisternal puncture is considered necessary it is recommended that ventricular puncture should be carried out as a pre liminary

Ventricular Puncture In cases of obstructive hydrocephalus

prognosis a progressive return of reducing power for some consecutive days being a sign of recovery

Lumbar puncture This procedure is necessary in cerebro spinal fever for diagnosis and for the relief of pressure Except in small children who can be held a general anæsthetic is advisable and gas and oxygen is very satisfactory Apart from its other advantages the general anæsthetic is said to increase the yield sometimes to fourfold of the fluid withdrawn drainage being thus promoted In performing lumbar puncture the patient is laid on his side the knees drawn up and the head and shoulders bent forward so that the back is arched and the interspinous spaces widened The patient should be so arranged that the lumbar region is on the edge of the bed The puncture is made in the space between the third and fourth lumbar vertebræ the body of the latter being deter mined by a line joining the iliac crests Having selected the intervertebral space the skin is thoroughly prepared and with all aseptic precautions the needle is carefully and firmly pushed in the mid line of that space just above the upper margin of the lower vertebral body At a certain point in the process of introducing the needle a characteristic give is noted as the point pierces the dura The stilette is then withdrawn and if successful fluid will well out If no fluid is obtained a little manœuvring of the needle by gently twisting it or pushing it a little further in may be successful It is essential that the needle should be introduced at right angles to the plane of the back otherwise the objective is missed and the point becomes engaged in the bony processes of the spine When the fluid spurts out the flow should be controlled by inserting the stilette for a suitable distance into the needle Unless only a few drops of turbid fluid escape showing that the fluid is practically pure pus the operator should not be discouraged by failure of a first effort and it may be necessary to renew the attempt after withdrawal of the needle or try the next space higher up *In children the needle will only require to be inserted for about ¾ of an inch* whilst in adults it may be 3 or 4 inches and in order to judge the distance some operators employ a needle graduated in ¼ inches or centimetres

Cisternal Puncture This is carried out with the same aseptic precautions as lumbar puncture the occipital region

pressure and contain an excess of polymorphs while prolonged search under the microscope or culture may reveal a Gram negative diplococcus Again in epidemics a small proportion of cases will be of the fulminating type in which though the patient is desperately ill meningeal signs may be equivocal and the cerebro spinal fluid clear A purpuric rash may give the clue to these In sporadic cases whilst the diagnosis of acute meningitis may be arrived at without much difficulty it must be remembered that there is hardly a pathogenic organism which at one time or another has not been numbered among the causal agents of this condition Commonest among these are the *streptococcus* and *pneumococcus* and should there be additional clinical evidence of infection due to one or other for example ear disease in the case of the former this would be strong presumptive evidence of the nature of the meningitis Cases not infrequently arise however in which the primary focus of such infections are obscure or overshadowed by the meningitis and lumbar puncture followed by bacteriological examination of the fluid will alone supply the diagnosis Apart from pneumococcal and streptococcal meningitis *tuberculous* meningitis may resemble the meningococcal variety In this case the onset is much more insidious and the history and general clinical examination may give the clue to diagnosis Nevertheless cases of tuberculous meningitis come under observation in which there has been no previous illness and signs of other tuberculous foci scanty or absent Again lumbar puncture will resolve difficulties The distinction between *benign lymphocytic meningitis or acute aseptic meningitis* and meningococcal meningitis may be very difficult to make and there seems little reason to doubt that in the past cases of the former have been regarded as meningococcal meningitis Clinically the signs may be identical and although this is disputed by many the position is complicated by the fact that in aseptic meningitis the cerebro spinal fluid may show polymorphs predominating at the outset Usually however the cells content is mainly lymphocytes The latter point together with the absence of organisms from the fluid either on microscopic or cultural examination would serve to differentiate the condition from meningococcal meningitis Other acute infections of the central nervous system such as

due to the block age of the ventricular foramina this method of drainage may be carried out but as in the case of cisternal puncture the introduction of chemotherapy has rendered it almost superfluous In infants in whom the fontanelles are not closed, after shaving and preparation of the scalp the needle is introduced at the lateral angle of the fontanelle in a plane parallel to the coronal sutures and directed slightly inwards towards the mid line for a depth of about 3 cm The stilette should then be withdrawn and if no fluid comes out the needle should be cautiously advanced for a few millimetres at a time until a depth of 4 cm is reached the stilette being removed each time to see if fluid is coming out It is most important not to change direction when the needle is in the substance of the brain and in the event of this being necessary the needle must be completely withdrawn and a fresh attempt made In patients with closed fontanelles the skull requires to be drilled by an apparatus such as that devised by Purves Stewart (1925) at the site recommended by Riddoch (1935) for ventriculography The landmarks are three quarters of an inch above the superior curved line of the occipital bone and 1 inch from the middle line After the opening in the skull has been made the needle is slowly pushed forwards horizontally and slightly outwards until on withdrawing the stilette the exit of fluid shows that the ventricle has been reached The head is then tilted backwards to encourage drainage

Diagnosis In epidemics the sudden onset of a febrile attack with acute headache vomiting a petechial rash head retraction and a positive Kernig s sign point to meningococcal meningitis with great certainty Muscular spasm in infants however is not always well marked in the early stages and such signs as neck rigidity and Kernig may not be readily elicited Again head retraction in infants may be misleading as they may adopt a similar attitude in various conditions not associated with meningeal involvement Those with pyrexia vomiting sudden attacks of screaming and especially if such a combination of signs is associated with squint should be carefully examined when usually some degree of neck rigidity can be made out Lumbar puncture will usually put the matter beyond dispute since although in the early stages the fluid may be almost clear it will be under increased

clearly at the various age periods the improvement since chemotherapy was employed During the period 1920–37 all cases were serum treated whilst during 1939–41 sulphapyridine only was administered

Comparison of Case Fatality Rates in Cerebro Spinal Fever by Age Groups in 1920–37 *and* 1939–41

	Age Group	0-1	1-4	5 9	10 14	15 19	20 29	30 39	40 49	50+	Total
1920–37	Total	128	97	31	6	8	38	19	8	8	383
	Died	111	67	16	11	13	0	1	6	7	[illegible]3
	Percentage died	87	69	52	42	46	53	63	75	87	68 7
1939–41	Total	64	11	45	43	57	63	3	1[illegible]	4	500
	Died	17	30	4	—	—	3	4	8	[illegible]4	90
	Percentage died	27	27	9 0	Nil	Nil	5	7	53	58	18

From an examination of the sulphapyridine treated group it will be apparent that the *age* of the patient is by far the most important factor in prognosis Case fatality is high in the first five years of life drops in the second quinquennium disappears altogether in the second decade rises again between twenty and forty until it reaches its maximum in the fifth and subsequent decades To those with much experience of cerebro spinal fever in the pre chemotherapeutic era the most striking feature of these results is the complete absence of fatality between ten and nineteen years and a more detailed analysis at the various yearly periods showed that among 107 patients aged eight to nineteen years not a single death occurred Again taking all cases 261 between the ages of eight and thirty nine we have the moderate fatality of 4 2 per cent Other factors affecting prognosis in sulphapyridine treated cases are *sex* presence or absence of *rash* and *day of disease* on which treatment is commenced With regard to sex males showed a better recovery rate than females Again patients showing the characteristic rash had a poorer chance of survival than those without the fatality of the two groups being 21 4 per cent and 16 6 per cent respectively The day of disease on which treatment was commenced was also of some effect on the end

epidemic encephalitis, acute poliomyelitis and *encephalomyelitis* in association with infectious disease may require consideration in differential diagnosis At their onset these may present certain resemblances to meningococcal meningitis but except in the early stage of the meningitic type of poliomyelitis in which the cells at first are polymorphonuclear the cerebro spinal fluid in these three infections will show mononuclears predominating The condition known as *meningism* found in acute infections such as influenza typhoid fever small pox scarlet fever B coli pyelitis or pneumonia may also stimulate meningitis Ker states that in such cases Kernig s sign is usually absent and the cerebro spinal fluid remains clear and sterile In *subarachnoid hæmorrhage* the clinical picture of acute meningitis may be exactly simulated but on lumbar puncture blood will be found in the cerebro spinal fluid while the white cell count will correspond with the amount of blood Or again the fluid will be yellow in colour from the presence of blood pigment

Prognosis Since the introduction of the sulphonamides the subject of prognosis in meningococcal meningitis has required complete reconsideration When the intra thecal administration of serum was introduced in the 1907 epidemic Ker in Edinburgh reduced his hospital mortality from 80 to 37 per cent and Robb in Belfast had similar success In the years following the 1914–18 war however the results obtainable from this method of treatment were disappointing and depended on various factors Cases coming early under treatment did better than those coming late patients between the age of five and twenty years had a much better chance of survival than those in other age periods whilst the prognosis in infants under one year and in tho e over forty was gloomy in the extreme also those with Group I infections had almost twice as great a recovery rate as with Group II infections Under all circumstances Sturdee (1936) gave a case fatality of 37 per cent but this was superior to that prevailing at the Edinburgh City Hospital from 1920 till 1937 when the case fatality in 383 cases was 68 7 per cent Since the introduction of the sulphonamide group the chances of recovery at all ages have been enhanced so that a recovery rate of over 80 per cent should now be obtainable The following table shows

such as nerve deafness neuritis or arthritis Nerve deafness must be regarded as serious for once begun it seems to progress rapidly to permanent stone deafness in one or both ears although complete loss of function is not incompatible with partial or even complete recovery In neuritis prognosis must also be guarded as recovery even partial is slow in declaring itself whilst in some cases the loss of function is permanent Recovery is to be expected in the majority of those exhibiting psychological complications particularly if early recognised and if active measures of rehabilitation are undertaken Whilst most cases of arthritis yield to treatment the possibility of permanent disability in the occasional case must be borne in mind

Prophylaxis Cerebro spinal fever is a notifiable disease and patients should be isolated in hospital on account of the necessity for skilled medical and nursing attention rather than on the grounds of prevention of spread School contacts should be excluded from school for three weeks but since the percentage of temporary carriers among contacts may be very high routine bacteriological examination of the e apart from its scientific value will yield little practical information on which to base administrative action Contact carriers should be given one or other of the sulphonamide compounds in a daily dosage of 3 gms for four days In institutional out breaks the first step is to secure thorough ventilation especi ally in sleeping quarters where the beds should be at least 3 feet apart and more if possible Measure should also be taken to prevent the aggregation of inmates at work play or at meal times Active immunisation by vaccines has been attempted but according to F G D Murray the result afforded little evidence of protection During an epidemic in Cyprus however Macalen and Bevan (1939) after carrying out active immunisation with heat killed vacciness believed that their results were good enough to warrant a further trial in future epidemics

Treatment In nursing the patient every precaution should be taken to keep him warm and to preserve the skin To the latter end an airbed should be employed and assiduous attention paid to pressure points Diet should be fluid and as nourishing as possible and if coma or opisthotonos are pre ent

result although the statistical evidence on this point was not so clear as could be desired Nevertheless the fact that cases treated on the first day showed a case fatality of 7 6 per cent as compared with 17 5 18 8 and 25 3 per cent when chemo therapy was begun on the second third and fourth days respectively shows that prognosis is improved by early treat ment The cases of cerebro spinal fever treated by sulphon amide in our experience have been almost entirely Group I infections but in a few Group II infections the results have been comparable with those in Group I although it might be well to await further information on this point In the individual case prognosis is affected by such circumstances as the mental condition and vomiting In those comatose from the first or wildly delirious the outlook is grave although not by any means hopeless for we have observed the most un promising cases of this type almost symptomless in four or five days Continuous vomiting which precludes oral adminis tration of the drug is also an unfavourable sign but again this may be overcome by perseverance with injection or by employing some other member of the sulphonamide group Temperature and pulse rates are uncertain guides in fact temperature curves may be misleading since sulphapyridine may exert an antipyretic effect in certain cases without pro ducing any measurable action on the infecting organism With the diminution in delirium or coma mental confusion vomiting headache and rigidity the patient can be confidently predicted to make a good recovery especially if he reaches the tenth day of illness with these signs of improvement as in our series of sulphapyridine treated cases 84 per cent of the deaths occurred on or before this day of disease In cases which seem to be hanging fire bacteriological and cytological examination of fluid obtained on lumbar puncture will supply the necessary information regarding the progress of the infection while the estimation of sugar will be most helpful in prognosis An increase in the amount of reduction of the copper salt is hopeful even when signs of clinical improvement are delayed as for example in children when the gun hammer position is main tained although the patients are taking the drug and fluids satisfactorily As we have seen complete recovery may be marred in a minority of cases by the occurrence of complications

clu ion reached by the group of Scottish workers (1943) who investigated the effect of sulphanilamide sulphapyridine and sulphathiazole on fatality rate and duration of stay in hospital of recovered cases Our personal experience with sulpha diazine and sulphamethazine would not place them higher than the others in effectiveness and at present therefore our choice would probably lie between sulphanilamide and sul phathiazole

Mode of Administration To be effective sulphonamide should be given in maximum dosage at the outset and during the first forty eight hours we administer from 3 to 11 grms per day according to the age of the patient and continue the drug treatment according to the scale of dosage set forth in the following table

Scale of Dosage of Sulphonamide in Cerebro Spinal Fever

D y	1		3	4	5	6	7	8	9	10
Twelve years and over	11	9	6	6	3	3	3	1 5	1 5	1 5
One to twelve years	7	6	3	3	1 5	1 5	1 5	0 75	0 75	0 5
Nil to one yea	3	3	1 5	1 5	0 75	0 75	0 75	0 75	0 75	0 5

Compared with that employed by other workers the dosage is high especially in the initial stages but it is felt that so long as these amounts are tolerated the greater amount that can be given the better The criticism that a wider range of dosage for the various age groups might be advisable and this is especially the case in the one to twelve age period is met by the argument that it is in the early years of this group one to five that the case fatality is high and accordingly the necessity for pressing the drug within the limits of safety is very great In those over twelve treatment is begun with an intravenous injection of 2 0 gms and in those between one and twelve with a similar injection of 1 0 gm of soluble sulphonamide There after the total daily amount is divided into two hourly doses given by mouth for the first forty eight hours and in four hourly doses for the second forty-eight hours Sub equently the drug is given three times a day till the end of treatment In infants the initial intravenous dose is omitted the drug

feeding by the nasal tube and intravenous glucose may be required Whilst it may not be possible in present-day hospitals in which the bull of patients must be accommodated in large wards it is undoubtedly a great boon to the cerebro spinal fever patient to be treated in a room by himself where he can be free from all extraneous noise For the relief of restlessness and delirium in children hot baths are useful but in adolescents and adults the practitioner should not hesitate to prescribe freely full doses of morphine and hyoscine compound until chemotherapy has done its work Attention to the toilet of the eyes and mouth is necessary whilst a careful watch must be kept on the bladder Herpetic lesions will also require treatment

Chemotherapy The serum treatment of cerebro spinal fever is now only of historical interest and while some have con tinued its employment in conjunction with chemotherapy, practically all are content to abide the results obtained by the latter alone Sulphonamide compounds were shown experi mentally by Buttle and his co workers (1936) and Proom (1937) to have a high protective value in meningococcal infections in mice and the demonstration by Marshall and his co workers (1937) that they would readily pass from the blood into the cerebro spinal circulation of patients suffering from meningo coccal meningitis was early made use of in treatment

The experience of clinicians in the widespread epidemics of cerebro spinal fever in the United Kingdom in 1940 and 1941 confirmed preliminary impressions of the efficacy of the sulphonamides so that until the advent of penicillin their employment in treatment became the accepted routine As far as chemotherapy is concerned therefore the only remaining consideration is as to which of the various members of the sulphonamide group preference should be given In our own *experience* both *sulphanilamide* and *sulphapyridine* have given excellent results but the toxic effects of the latter in the shape of a tendency to cause rashes and gastric troubles led to the adoption of sulphathiazole and sulphadiazine which are better tolerated by the patient Some discussion has arisen as to the therapeutic efficiency of the various sulphon amides but it is doubtful if any are more active than the sulphanilamide originally employed and this was the con

days of treatment and this interval between onset and time of appearance suggests an etiology similar to that of serum sickness. They appear as generalised erythemata on the face trunk and limbs and almost invariably are morbilliform or rubelliform in character The resemblance to the rash of measles and rubella is so close that at times diagnosis is most difficult especially as pyrexia of 100 or 101 F is often found with the rash and occasionally some facial oedema as well When the rash begins to fade an urticarial or circinate pattern may appear to give a clue to the nature of the erythema *Drug fever* as a sole effect of any of the drugs is also relatively common but as it is not always possible to exclude with certainty other causes for an elevation of temperature we were unable to estimate the incidence in our sulphapyridine cases Usually disclosed by a sharp rise in temperature lasting from two to four days it may be indicated by a niggling pyrexia lasting for a week and be accompanied by general malaise and depression Infants often become exceedingly irritable *Urinary complications* appeared in only 4 out of 500 consecutive sulphapyridine treated patients and consisted of temporary anuria in 1 case albuminuria in another and haematuria in 2 They occurred from the seventh to the ninth day of treatment and with the withdrawal of the drug and the increase in fluid intake they cleared up in a few days *Blood changes* in the shape of granulocytopenia have now been reported in many conditions treated by sulphonamides but apart from an occasional leucopenia which was relatively transient no serious effect on the blood forming tissues was encountered in the large series of cases mentioned Nevertheless the possibility of the onset of granulocytopenia should always be borne in mind during chemotherapy and should blood examination

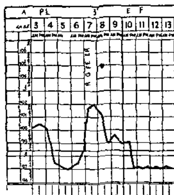


FIG 36 Temperature chart of sulphapyridine treated case of cerebro spinal fever showing drug fever lasting from fifth to eighth days of treatment

being given orally from the beginning two hourly for the first forty eight hours four hourly for the second forty eight and three times a day thereafter For oral administration the tablets are crushed in milk The main obstacle to giving the drug by mouth is vomiting and when this interferes with treatment recourse must be made to intravenous and intra muscular injection until vomiting is brought under control In stuporose patients or in those in whom marked opisthotonos interferes with swallowing the drug is given by the nasal tube Apart from lumbar puncture for diagnostic purposes spinal tap has been given up except in cases which seem to hang fire and cisternal and ventricular puncture have practically passed out of use in treatment *The intraspinal introduction of any of the chemotherapeutic agents commonly employed in the treatment of cerebro spinal fever not only does not appear to offer any advantage but is definitely dangerous* It is essential during the administration of sulphonamide to see that the patient is given abundant fluids at least 4 pints per day for adults and we give McLean s alkaline powder as a routine to all patients Some have stressed the necessity for the control of treatment by the estimation of sulphonamide concentration in the blood but the attainment of a satisfactory level in this respect i e a minimum of 5 mg per cent will not necessarily guarantee a successful result and careful observation of the patient will usually give all the information necessary to decide whether or not he is responding to treatment If not then the administration of the drug by injection should be carried out for a period to eliminate the possibility of failure to absorb from the alimentary tract

Various *toxic effects* fall to be considered in connection with treatment by sulphonamides and whilst the following account is based on our experience of sulphapyridine treated cases it should be noted that any of the sulphonamide derivatives may give rise to the side effects considered *Drug rashes* are held to be commoner after the use of sulphanilamide than others of the series but in our sulphapyridine treated cases they were relatively common occurring in 7 per cent of the cases They were more often seen in males than females, and two thirds were distributed over the five to thirty age period The usual time of appearance is from the ninth to the eleventh

is treated on the usual principles In our experience no obvious benefit is derived from the administration of vitamin B in large doses There appears to be no treatment for nerve deafness When the occurrence of relapse has been verified by lumbar puncture energetic chemotherapy should be instituted at once

Penicillin Since this substance became available we have employed it in a number of patients especially children under five years of age in whom fatality after chemotherapy is still not negligible Given simultaneously by intrathecal injection and continuous intramuscular drip the results have been less favourable than those obtained by chemotherapy and indeed one or two patients who failed to improve on penicillin responded at once to sulphonamides Patients who recover under penicillin are slower in showing signs of clinical improvement than with chemotherapy and the temperature settles less quickly At this early stage therefore we believe that chemotherapy is the treatment of choice in cerebro spinal fever

disclose its occurrence the drug should be withdrawn and pentose nucleotide given at once *Cyanosis* resulting from methaemoglobinemia or sulphaemoglobinemia is frequently seen during the course of treatment with sulphanilamide and less often with the other sulphonamides Subjective phenomena such as *digestive disturbances* and *depression* are difficult to assess Many patients complain of nausea but with encouragement will manage to retain the drug A sense of fullness in the epigastrium flatulence and epigastric discomfort are common but disappear with the progressive reduction in dose Mental depression is also often marked, and one medical patient referred to this as almost the worst feature of the whole illness Vomiting has already been referred to as one of the cardinal signs and it is impossible to decide how much of this is a manifestation of the disease in the early stages and how much of it results from chemotherapy If however the drug is persevered with it is remarkable how vomiting disappears and this alone is not a deterrent to its use as has been our experience with sulphonamide treatment in some other conditions such as pneumonia Deep sterile *abscesses* resulting from the intra muscular injection of soluble sulphonamide although not strictly speaking a side effect of the drug are undoubtedly a drawback to the employment of this method They take a considerable time to heal and delay convalescence but in certain cases the risk must be taken otherwise the use of a most effective remedy will require to be abandoned In any case when the precaution is taken of diluting the drug in solution with three times its volume of sterile distilled water the occurrence of abscesses is not very common Taken all over and considering the large total amounts of the drugs given to our cases we have seen no toxic effects which could be held to be serious contra indications to their employment Indeed it is not too much to say that cerebro spinal fever patients tolerate sulphonamide very much better than any other class of patient in whom we have found it necessary to employ chemotherapy

Complications should be treated on general lines Thus arthritis will usually respond to rest and physiotherapy and possibly a further course of sulphonamide but in severe cases the advice of the orthopedic surgeon should be sought Neuritis

changes are characteristic A leucopenia with a relative lymphocytosis is very constant probably as a result of the proliferation of the causal organism in the bone marrow Following infection immune bodies appear in the blood the most important of these from the clinical point of view being the agglutinins which are demonstrated by the Widal test Agglutinins appear in practically all cases at one time or another being scanty or absent in the first week reach their maximum about the third week and after the fourth week begin to diminish Weil and Felix (1920) introduced a refinement in agglutination methods by the introduction of qualitative agglutinin analysis in which a distinction is made between flagellar (H) and somatic (O) agglutinins and in any given case it may be necessary to study both forms It is claimed that still further precision ha been added to serological procedures in enteric infections by the demonstration of the Vi antigen by Felix and Pitt (1934) By an agglutination reaction certain typhoid cultures can be shown to contain this antigen and such cultures are employed in the investigation of the corresponding antibody Complement deviating antibodies appear also and while their estimation is not now much employed in clinical work especially since the discovery of O agglutination nevertheless their demonstration may be helpful on occasion The post mortem findings are chiefly those of inflammation and the characteristic ulceration of the ileum the ulcers being oval in shape with the long axis parallel to that of the bowel and showing unindurated edges There is also enlargement of the mesenteric glands and spleen Other appearances depend on the nature of complications Thus a general peritonitis may be present following perforations of the small bowel whilst pneumonia and empyema ulceration of laryngeal cartileges inflammatory or suppurative lesions in kidney gall bladder and other organs may all be additional features The heart muscle is also usually pale and flabby

Etiology The epidemiological features of enteric fever as far as the distribution between typhoid and paratyphoid infections is concerned has undergone a marked change in the United Kingdom since the war of 1914–18 Before that event practically all cases were true typhoid fever but of recent years paratyphoid B infections have predominated

CHAPTER VII

ENTERIC FEVER

Nomenclature Enteric fever includes the typhoid and paratyphoid fevers which in their essential clinical features are exactly alike The gross pathology is the same serological and biochemical investigation of the causal organism alone enabling a distinction to be made

Pathology The causal organisms of enteric fever are Bact typhosum or Bact paratyphosum A B or C whilst on occasion mixed infections are found Infection is by ingestion and it was originally believed that enteric organisms passed directly to the small intestine set up a characteristic hyperplasia in the lymphoid tissue and from there invaded the blood stream Modern pathologists postulate a more devious route of invasion of the tissues After ingestion the organisms pass to the intestine and at once from there to the mesenteric glands They then find their way by the thoracic duct to the blood stream to set up a bacteriæmia which however is transient but the organisms carried to the liver spleen gall bladder and bone marrow proliferate in these organs This phase corresponds clinically to the incubation period A secondary bacteriæmia now ensues and gives rise to the signs and symptoms of the invasion period In addition there is an invasion of the intestine from the gall bladder in which free multiplication of the organisms has taken place This results in ulceration and necrosis of Peyer s patches and the intestinal lymph nodes Also during the secondary bacteriæmia the pelvis of the kidney may be invaded Persistent foci of infection may remain in the gall bladder and kidney after clinical recovery in which event the patient continues to excrete organisms and becomes a chronic fæcal or urinary carrier In addition to these processes which are the result of invasion by one or other of the enteric organisms secondary invaders such as the pneumococcus or streptococcus produce complications *e g* those found in the lung Effects on the central nervous system and degeneration of the myocardium are usually the result of toxæmia In enteric fever the blood

examples of widespread and explosive outbreaks although sporadic cases appearing over a long period of time may also be due to a water supply receiving occasional contamination Many observers e g Ritchie (1937) have pointed out an interesting feature of some of these namely that they are preceded immediately before by a high prevalence of gastritis and enteritis resulting from the vast bacterial flora found in sewage contaminations *Mill* also may transmit infection the source of infection being a carrier who is concerned in milking the cows or handling the milk but outbreaks have been traced to the washing of milk containers with polluted water or even to the adulteration of milk with contaminated water Scott (1937) has made the suggestion that on rare occasions enteric might prove to be a bovine disease resulting in milk infection In addition to milk which in the form of ice cream has proved to be a vehicle of transmission various other food stuffs may act in similar fashion Among these are *shellfish* gathered from sites polluted with sewage effluent green *salads* or *watercress* grown in soil exposed to contamination with human excreta whilst *cooked meats* prepared in unhygienic conditions or handled by a carrier of enteric organisms may be infected at some stage of preparation or distribution Even loaves of *bread* contaminated in the latter way were strongly suspected to be the means of transfer in a Liverpool outbreak Since ambulant cases of the paratyphoid B fever are relatively common it is possible for quite extensive food outbreaks of this to be set up by food handlers suffering from this form of the disease In undeveloped regions where sanitary standards are low there can be little doubt of the importance of *flies* and *dust* as disseminators of infective material The mode of infection is by ingestion

Infectivity Apart from its wholesale transmission by water milk or food enteric is one of the classical examples in which spread is brought about by direct contact of the fingers with excreta By the adoption therefore of rigid aseptic nursing i e the use of gowns and the surgical cleansing of the hands after handling the patient scrupulous current disinfection of bed and body linen utensils and excreta of the patient there is no danger of spread Such conditions are however only likely to be realised in hospital and home nursing therefore

so that at the North Western Hospital Hampstead in the eight year period ending 1934 paratyphoid B accounted for 60 per cent of the total all but a few of the remainder being attributable to typhoid and in the Edinburgh City Hospital for the twelve year period ending 1938 paratyphoid B fever occurred in 73 3 per cent of enteric cases Paratyphoid A and paratyphoid C fever are rare in the United Kingdom The disease may occur in any climate the chief seasonal incidence in the United Kingdom being in the third quarter of the year No age escapes but infection is commonest in the ten to twenty five age period males being attacked slightly more frequently *than females Case fatality rates are very variable as between* one outbreak and another At the North Western Hospital from 1926–34 it was 4 3 per cent all deaths being Bact typhosum infections the case fatality rate in the latter being 9 per cent This individual experience however must be accepted with reserve as numerous paratyphoid epidemics have given as high mortalities as those in typhoid and a paratyphoid B outbreak in Liverpool is reported by Frazer and others (1937) to have shown a case fatality of 9 per cent The disease has become a strikingly reduced factor in mortality in England and Wales in the past sixty years Whereas in the five yearly period ending 1875 it accounted for 371 deaths per million per annum in 1938 it was 4 per million Incidence has also greatly diminished from 0 25 per 1 000 in 1911–15 to 0 8 per 1 000 in 1926–30 these decreases in mortality and incidence being largely the result of measures directed to the improvement of water supplies and sewage disposal Goodman (1933) has drawn attention to a further interesting feature namely that of recent years the preponderance of deaths and incidence has shifted from the large towns to the smaller towns and rural districts

Transmission The sources of infection are patients suffering from the disease including the mild and ambulatory forms and carriers The incidence of the latter among the general population has been estimated at 3 per 1 000 The infecting organism is excreted in urine and fæces and dissemination frequently occurs by *manual* transmission *Water* is a well known vehicle of infection drinking supplies on becoming contaminated with infected sewage having supplied many

Stage of Advance After a few days the patient takes to bed and about a week from the beginning of symptoms some of the more typical features of the disease are presented In appearance he shows a hectic flush and looks worn out He answers questions in a tired voice and hesitatingly and if left alone will resume his drowsy inertia The breath is foul the tongue dry furred fissured and tremulous sordes may be present on the teeth and lips and dirty mucus adheres to the inside of the cheeks and palate On examination the abdomen is tumid and if the disease is well developed the spleen will

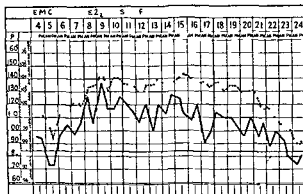


FIG 37 Temperature and pulse chart of case of typhoid fever showing typical temperature curve The pulse rate however remained high a common occurrence in patients of this age

usually be palpable although in some patients tenderness only in the splenic region will be made out The appearance of the rash marks the beginning of the stage of advance and in the average case this is found scattered about the abdomen the lower part of the chest and irregularly on the back It may however vary greatly in profusion in some being represented only by several equivocal spots on the abdomen which may be missed unless carefully looked for in a good light whilst in the few in which it is very profuse it may be found covering the whole of the trunk and the proximal part of the limbs In character the rose spots of enteric are maculo papular disappear on pressure each lasts for three or four days and fades to a brown colour before disappearing They continue to come out for a variable period during the second and third

can rarely be justified It is also easy to understand that in the absence of proper precautions spread may occur quite readily especially among those of imperfect habits of personal cleanliness or in overcrowded insanitary dwellings With regard to the duration of infectivity it would be reasonable to regard a patient as potentially infectious from the moment the organism establishes itself in his body and he remains so until clinically well By the time the latter stage is reached in the greater number of cases the tissues have cleared themselves but in a certain proportion they fail to do this and a convalescent carrier stage is established which may persist for years In practice therefore it is customary to obtain at least two consecutive negative cultures from stools and urine before the patient is regarded as free from infection

Incubation and Quarantine Period The incubation period is somewhat variable the outside limits usually given being from two to twenty-one days with ten to fourteen days as the common time The imposition of quarantine on contacts is not as a rule employed in enteric infection in these usually being determined by bacteriological examination of stools and urine

Clinical Features Stage of Invasion Whilst cases of abrupt onset are occasionally noted in general this is most gradual a stage of invasion lasting for about a week occurring in most cases During this time the patient s general reactions are such as might be associated with any febrile disturbance and include headache loss of appetite malaise chilliness or rigors vague pains all over the body and at night in spite of his weariness the patient is restless sleepless and perspires freely These general disturbances may be accompanied by abdominal discomfort or even pain sometimes referred to the right iliac fossa Constipation is the rule at this stage but diarrhœa may be present Cough is often a troublesome feature and epistaxis occurs in a fair number of cases Starting then from a mere feeling of out of sorts these various symptoms and signs accumulate and with the passage of each day the patient s general condition deteriorates As it does so the characteristic temperature curve discloses itself rising in step ladder fashion each evening showing a greater rise than the preceding with an intervening morning remission The pulse remains relatively slow but the respirations may be a little accelerated

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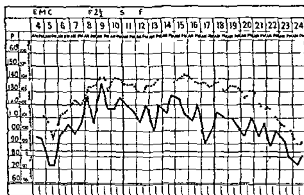


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Immediate death may occur but the patient may be tided over the crisis and fortunately copious bleedings do not often recur although in his exsanguinated state he may fall a more ready victim to exhaustion and heart failure *Perforation* of recent years has been seldom seen in our experience and at the North Western Hospital occurred in only about 2 per cent of cases but when it occurs it is more to be dreaded than hæmorrhage It is usually found in the terminal part of the small intestine and early signs of diagnostic importance are shivering slight increase of muscular rigidity of the anterior abdominal wall and quickening of the pulse rate The *onset however is frequently* marked by some degree of pain This may be sudden and severe especially if the mental condition of the patient enables him to report it and even in those in the stupor of the typhoid state some indication may be obtained from tremulous movements of the hands towards the abdomen drawing up of the knees or feeble *moaning* The *temperature drops* suddenly the pulse accelerates and these changes may be accompanied by rigors and vomiting The anterior abdominal wall becomes tender and rigid respiratory movement is absent and the picture of general peritonitis is soon complete Owing to the necrotic condition of the bowel surgical treatment is not very hopeful and the condition is frequently fatal Besides these two main dangers others may appear about the same stage of the disease *Meteorism* or *diarrhœa* in the shape of excessive *looseness may accelerate exhaustion or* be a precursor of hæmorrhage or perforation *Hypostatic pneumonia* may result from excessive weakness and *toxæmia* may be so profound as to bring about death from heart failure

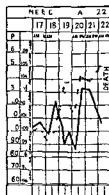


Fig 39 Temperature and pulse chart of case of typhoid fever showing perforation Note drop in temperature and increase in pulse rate Operation was carried out within two hours of first sign of perforation but death occurred

Stages of Defervescence and Convalescence About the end of the third week in a typical case the temperature begins to

weeks of a typical case. Constipation, although it may remain obstinate in this stage, is usually replaced by the passage of characteristic "pea soup" stools, which contain fragments of undigested food and occasionally shreds of mucous membrane. The temperature has now reached its acme and runs between 100° and 104° F with fluctuating morning remissions. The pulse is relatively slow, in the neighbourhood of 90, with probably a dicrotic element, and the respirations are usually accelerated to 26 or 30. Remaining in this condition for one or two weeks the patient wastes rapidly. Looseness of the bowels continues, he becomes incontinent and lies exhausted, stuporose or semi-delirious in a state of complete helplessness. The pulse becomes weak and definitely dicrotic, and the typhoid state may be reached, in which wasting and debility are extreme, with subsultus and picking at the bedclothes. Towards the end of this stage necrosis of the bowel commences

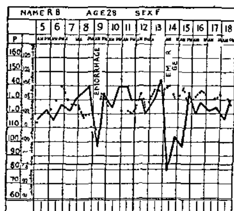


Fig 38. Temperature and pulse chart of recovered case of typhoid fever showing hæmorrhages on the ninth and fourteenth days. Note well marked drop in temperature coinciding with hæmorrhage in each case.

and consequently hæmorrhage or perforation may take place. *Hæmorrhage* is the more frequent, and in our experience at the North Western Hospital was found in various degrees in about 7 per cent of patients. It is more prone to occur in adult males than others and varies considerably in amount. There may be only faint streaking of the stool or the voiding of one or two small clots. Greater degrees may be marked by a fall in temperature and subsequent passage of tarry stools and larger clots, and if this continues the patient rapidly goes downhill. Or again a sudden severe hæmorrhage may result in a gush of blood per rectum accompanied by collapse, sighing respirations and a sudden drop in temperature

better after the condition had lasted for some months *Suppurative arthritis* is also occasionally a complication

Cardio vascular Complications Of these the commonest is *thrombo phlebitis* which indeed in our experience is the most frequent of all enteric complications The characteristic white leg appears during defervescence or convalescence and usually proceeds to complete recovery In well marked attacks some degree of *myocardial degeneration* is almost invariably present resulting in various degrees including the fatal form of circulatory failure *Endocarditis* and *pericarditis* are also occasionally found

Upper respiratory tract infections have not been uncommon in our experience in the shape of *tonsillitis adenitis* and *otitis media* *Parotitis* unilateral in distribution and sometimes suppurative in character may occur in severe cases

Urinary Complications *Nephritis* appearing concurrently with the onset of the disease has been reported but in our experience *albuminuria* and *nephritis* in the later stages are much more likely to be encountered *Pyelitis* and *cystitis* may also be associated with enteric and persistent foci in the pelvis of the kidney account for the carrier state in some individuals

Nervous Complications Of these *tender toes* are relatively frequent and may cause acute distress to the patient Many nervous complications such as *cerebral thrombosis* and *embolism neuritis meningitis myelitis* and *encephalitis* have been described in enteric but they are rare *Meningismus* is however relatively common Some degree of mental weakness lack of concentration and emotionalism is seen on recovery from long and exhausting illnesses

Gall bladder Complications *Acute cholecystitis* may occur at any stage of the disease or in convalescence but it is unusual Organisms of the typhosus paratyphosus group are occasionally found in gall stones removed at cholecystectomy performed for conditions apparently unrelated to enteric and in a large proportion of persistent intestinal carriers the organisms are harboured in the gall bladder

There is no particular association between enteric and other infectious or non infectious diseases

Relapse and Second Attack Relapses are well known phenomena in enteric occurring in about 10 per cent of cases

break shows well marked morning remissions and gradually comes down by lysis The abdomen loses its tumidity the spleen recedes the expression becomes more alert and the appetite may be little short of ravenous The temperature however tends to be unstable until convalescence is well established dietetic indiscretions or constipation being readily reflected in excursions on the charts With return to normal the patient soon regains weight almost visibly sometimes and strength slowly returns Convalescence is usually prolonged and may last from one to three months according to the severity of the attack

Complications Nearly every tissue has been reported as the site of an inflammatory lesion of greater or less degree in enteric and considering that we are dealing with what may be a long and exhausting illness which commences with a generalised blood infection this is not surprising It is probably best to group complications according to their occurrence in various systems

Respiratory complications are not infrequent and *bronchitis* is a characteristic feature of the disease in many cases *Laryngitis* with *perichondritis* and *ulceration of the cartilages* may show itself in convalescence with a very insidious onset and is of dangerous import *Lobar pneumonia* sometimes present at the onset may occur at any stage while *pleurisy* with effusion or *empyema* is also occasionally found *Hypostatic pneumonia* is often to be noted in the severe forms of infection

Bone and Ligament Complications *Periostitis* is a characteristic complication occurring in convalescence the incidence being chiefly in the tibia ribs and femur although we have seen one unusual case in which it occurred on the anterior surface of the cervical vertebræ and gave rise to a post pharyngeal abscess Periostitis may be accompanied by osteitis and necrosis of bone *Typhoid spine* although comparatively rare is definitely associated with enteric and according to the Keiths (1926) results from the deposit of bony tissue round the vertebral bodies and into the intervertebral discs and vertebral ligaments Clinically it is shown by rigidity of the lower spine pyrexia girdle pains shooting down the sciatic nerve incontinence of urine and exaggerated knee jerks The only case we have seen went out of hospital very little

about three weeks The disease tends to take this form in children in whom the rash is often absent while on the other hand enlargement of the spleen is frequently well marked On one or two occasions we have encountered an *afebrile* type of enteric in which the clinical picture was complete and the attack quite severe the temperature remaining sub normal throughout As in other fevers there is a fatal *toxic* type characterised by hæmorrhages from the nose mouth intestine kidney and into the skin Lastly from time to time the onset of what afterwards is seen to be enteric assumes at first the characters of a *pneumonia* a *nephritis* or a *meningitis* and to these varieties the terms pneumo nephro and meningo typhoid have been given

Paratyphoid Fevers The point has been much debated as to the relative severity of typhoid as compared with para typhoid fever Different epidemics of either infection vary greatly in severity as judged by case fatalities and complication rates but in our personal experience of endemic enteric in the post war period in London and Edinburgh there can be no doubt that the severer clinical forms are typhosus infections the great bulk of those due to the paratyphosus organisms being of the abortive and mild types Also in the latter the onset tends to be more abrupt the temperature curve tends to be atypical and complications though by no means un known are not so severe or frequent

Diagnosis It must be admitted that at the present time when enteric has become an uncommon disease and when it does occur it is apt to appear in an abortive or mild form the condition does not readily suggest itself Apart from a febrile disturbance with its usual concomitants there may be nothing tangible on which to base a diagnosis Or again in the early stages of a more severe infection clinical diagnosis may be a matter of some uncertainty but if febrile symptoms are associated with abdominal discomfort and particularly if these persist then bacteriological assistance in diagnosis should be sought When the disease presents the gradual onset a characteristic rash enlarged spleen tumid abdomen and dicrotic pulse some bronchitis and typical facies the diagnosis presents little difficulty

Differential Diagnosis In present day hospital practice

and may appear during defervescence or after an apyrexial period of a week or two At the present time we see them in about 4 per cent of cases They are more frequent in women and many observers have called attention to the association between the *onset of a relapse and menstruation* Generally relapses present a modified form of the disease but this is not necessarily so and they may be severe and fatal Second attacks are very rare

Varieties of the Disease The disease as described above may be taken as following a moderately severe course but mild types especially at the present time are common Of these

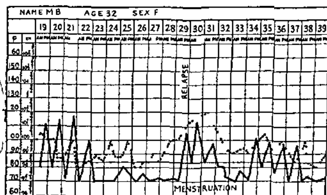


Fig 40 Temperature and pulse chart of case of typhoid fever showing mild relapse at menstrual period The commencement of the chart shows only the lysis of the primary attack

the *ambulatory* form causes the least restriction of the subject's activities the patient believing that he has nothing more than an attack of mild influenza and continuing with his occupation such cases sometimes only being discovered during the investigation of notified cases It should be realised that these are not entirely free from danger as hæmorrhage or perforation have been known to occur at the appropriate time in the disease *Abortive* types of enteric also occur in which the fever is shortened to a week or less and in these the clinical signs are not well marked diagnosis usually being made on bacteriological or serological grounds Again the main features may be well presented in the *mild type* with characteristic though scanty rash and a moderate febrile and constitutional reaction lasting

latter is seen in the early stage of advance the true nature of the illness being revealed by blood culture *Acute rheumatism* and toxic states such as *uræmia* and *diabetic coma* have also come under our notice as suspected cases of enteric as has *splenomegaly* resulting from various causes *Acute food poisoning* due to organisms of the salmonella group possibly because some article of diet is obviously implicated is sometimes thought to be enteric but the rapidity with which symptoms appear after the ingestion of food together with vomiting as well as profuse diarrhœa and collapse usually enable a distinction to be made *Undulant fever* has become of some medical interest in this country of recent years and the usual laboratory routine of including suspensions of Br abortus among the organisms tested for agglutination in cases of suspected enteric di closes cases of infection due to this organism from time to time A group of cases of *infectious mononucleosis* notified as enteric have come under our notice Among these several showed a rash more or less resembling the rose spots of enteric but the general appearance of the patient the typical lymphadenitis and the hæmatological examination showed the true nature of the condition Other acute infections such as *typhus* certain forms of *smallpox* and the typhoid type of *scarlet fever* are now largely of academic importance in differential diagnosis

Laboratory Diagnosis An absolute diagnosis can only be made when one or other member of the typhosus paratyphosus group has been isolated in pure culture from the blood stream and *blood culture* should be carried out in every case of suspected enteric if it is seen in the first ten days of illness Thereafter the chances of recovery of the organism are less hopeful but in well developed cases we have obtained positive blood cultures as late as the third week Organisms of the typhosus paratyphosus group can readily be isolated from the blood clot which forms in specimens of blood sent in a sterile container to the laboratory but if it is desired to inoculate a fluid medium most public health authorities will be prepared to supply a flask containing the appropriate medium and this should be inoculated with 5–10 c c of blood obtained in a record syringe after vein puncture under aseptic precautions The inoculated medium should then be delivered to the bacteriologist at once

obstinate *constipation* or various forms of *non specific enteritis* and *influenza* are more commonly mistaken for enteric than any other condition and careful observation for a day or two usually discloses the nature of the disturbance *Meningitis* due to the meningococcus streptococcus pneumococcus or B tuberculosis are also confused with enteric but the signs of meningeal irritation and the results of lumbar puncture should clear up the diagnosis always bearing in mind that mening ismus may be present or the remote possibility of the case being of the meningo typhoid type Various chest conditions such as *bronchitis acute lobar pneumonia pleurisy empyema* and *pulmonary tuberculosis* may also give rise to difficulties but again clinical observation and the help obtainable from laboratory or radiological procedures should make the position clear Acute abdominal conditions are occasionally diagnosed as enteric and vice versa and all who have any experience of enteric have probably encountered cases in which appen dicectomy has been embarked on the diagnosis being made at operation The localised pain tenderness and rigidity found in *acute appendicitis* are not very often found in enteric nor the acute onset with vomiting characteristic of the former In this difficulty a total white and differential cell count will be of assistance the leucopenia and relative lymphocytosis of enteric contrasting with the polymorph leucocytosis of appendi citis *Cholecystitis* has also been mistaken for enteric but the type and localisation of the pain in this condition is not char acteristic of enteric General infections such as *acute miliary tuberculosis* require to be distinguished from enteric and in the absence of previous history pointing to tuberculosis or of the characteristic X ray appearances of that disease it is doubtful if a positive diagnosis is likely to be made on clinical grounds during life although negative blood cultures and serological reactions would be strongly in favour of the case not being enteric *Malignant endocarditis* is another similar condition sometimes mistaken for enteric but this will usually present signs and symptoms pointing to the heart *Septicæmia* including the puerperal variety due to the hæmolytic strepto coccus with or without an obvious primary focus also on occasion will be difficult to distinguish from enteric with which of course it has much in common clinically when the

the course of the illness fail to give a positive Widal In the past diagnostic aid has been sought from the complement fixation reaction in the difficulties set forth above but now most reliance is placed particularly in respect of previously immunised persons on the demonstration of O agglutinins although Beattie and Elliot (1937) have found O agglutination with B typhosus and B paratyphosus B in dilutions as high as 1 in 160 several months after artificial immunisation A rising titre for O agglutination however is very significant or again if H agglutination is below significant titre and O agglutinins are present in any dilution then the presumption that the patient is suffering from enteric is very strong It is claimed that detection of the Vi antibody which except in carriers remains present for only a short time after recovery from the disease would also strongly support the diagnosis The characteristic blood count previously described may supply corroborative evidence of the presence of enteric

In the diagnosis of the *carrier state* Mackie and McCartney suggest that suspected individuals should be given a calomel purge followed by a saline the specimen for examination to be elected from the second or preferably the third loose motion Bacteriological examination of the urine should also be carried out A considerable number of carriers are stated by the same authors to give a positive Widal reaction and therefore the performance of this test may be of some value as a preliminary in the search for carriers those showing agglutination with dilutions of 1 in 20 or over for H or O agglutinins requiring stool and urine cultures Serological investigation for the presence of agglutinins for the Vi antigen has been proposed by Felix Krikorian and Reitler (1935) for the detection of permanent carriers Boyd (1939) believes that the test is likely to be of great assistance in bringing these to light but in temporary or convalescent carriers approximately half the cases failed to show Vi agglutination whilst another drawback was that until recently it could only be applied to typhosus infections Moreover Horgan and Drysdale (1940) could not establish a correlation between positive Vi agglutination and the carrier state

Another diagnostic refinement which may prove useful in epidemiological investigations has been introduced by the

for investigation The isolation of the organism from the *fæces* may also be attempted as a diagnostic procedure During recent years the method of isolating these organisms has been greatly improved and examination of the fæces is of the greatest diagnostic value at all stages of infection Organisms may also be isolated *from the urine and repeated* examinations may be necessary for this purpose If blood culture proves unsuccessful then a sample of blood should be obtained for the *Widal reaction* This should be per formed by a trained laboratory worker and not less than 5 c c of blood provided for the test The laboratory report as a rule will state the end titres at which agglutination occurs with both H and O antigens the criterion of a positive test being that H agglutination occurs in a typhoid infec tion in a serum dilatation of 1 in 60 or higher and in a para typhoid B infection in 1 in 120 or higher The finding of O agglutination even in low dilutions will usually mean that infection is present although it should be realised that occasionally indubitable typhoid infections will fail to show this H agglutination with paratyphoid A in dilutions of 1 in 30 may be regarded as a positive result In practically all cases a positive Widal reaction justifies the diagnosis of enteric and should the first test be inconclusive in respect of the end titre at which agglutination occurs then it should be repeated a rising titre for one of the organisms being highly suggestive of infection by that organism One negative result should not be regarded as excluding enteric unless on repeating the test in the fourth week it is again negative as agglutinin production appears to be delayed in some cases In addition to the difficulty of delay certain other factors remain to be reckoned with in assessing the diagnostic value of the test For example the patient may previously have suffered from enteric an unusual contingency or more probably have received prophylactic inoculations *In connec* tion with the latter it is possible that a person previously immunised against enteric on contracting a febrile illness other than enteric may show a rise in the agglutination titre for the enteric group of organisms the anamnestic reaction Lastly all clinicians are familiar with the unusual cases which though quite typical clinically and frequently examined in

diarrhœa are also unfavourable signs unless they yield to treatment Obviously such complications as pneumonia, pleurisy or nephritis must worsen prognosis and the only cases we have seen who contracted laryngitis were fatal As a rule the outlook in relapse is good In giving a prognosis in enteric it should be borne in mind that a certain proportion of recovered cases probably from 2 to 5 per cent will become convalescent carriers and this condition may persist for years particularly in females The effect of enteric on pregnancy is serious According to Ker this results in abortion or premature delivery in from one half to two thirds of cases while Goodall s experience is that enteric is a very serious event for the mother and that the prognosis for the child is very bad

Prophylaxis Community measures of protection against enteric include provision of pure water supplies routine supervision of milk and food with effective pasteurisation of the former and the proper disposal of sewage and refuse In cases of the disease notification disinfection of all articles with which the patient has been in contact including bedding and body linen and hospital isolation are carried out The latter is usually undertaken unless the home conditions of the patient are exceptionally satisfactory in that all facilities for the treatment and nursing of a severe and possibly long-drawn out illness can be undertaken and moreover under such conditions that the most complete precautions can be taken to prevent the spread of infection over this protracted period In investigating outbreaks all possible information should be sought in respect of obscure or transient illness in contacts and the sources of all articles of food or drink which have been partaken of in common by those attacked In urban communities where proper sanitation exists carriers are the chief means of spread and painstaking investigations may be necessary to disclose these

Active immunisation against enteric can be obtained by the injection of T A B vaccines For the preparation of these smooth strains of Bact typhosum Bact paratyphosum A and Bac paratyphosum B are selected and killed suspensions are put up so that usually 1 0 c c of the vaccine contains 1 000 million typhosum and 750 million each of paratyphosum A and B This is injected in two or three doses of 0 5 and 1 0 c c

work of Craigie (1938) who has differentiated thirteen bacteriophage types of B typhosus By this method a strain from a carrier or other source of infection may be typed and linked up with strains isolated from other cases

Prognosis Taken as a whole the prognosis in endemic enteric fever is not unfavourable as a reference to the case fatality rates already quoted will show, but in epidemics it is possible the risk of death may be greater The type of infection may not affect prognosis in the individual case a great deal but in general the outlook in a paratyphoid B infection is usually better than in typhoid Age would appear to be an important factor case fatality rates being lowest at the 5–10 age period the risk of death gradually increasing thereafter with age and being greater in adult males than females In individual cases prognosis depends on the assessment of the clinical condition of the patient If he can be roused and can undertake slight movements to assist himself in the course of his routine nursing treatment he is obviously in better shape than the semi delirious helpless case All authorities are agreed on the importance of careful observation of the state of the circulatory system and should the pulse rate exceed 120 in adults and the first sound become muffled the outlook is serious since the majority of deaths are due to heart failure resulting from toxæmia The main information to be derived from the temperature chart is in the amount of variation between the morning and evening levels The patient *who gets a good morning remission will generally* be doing better than he whose temperature shows little variation and provided the former is present a high temperature is in itself not necessarily a danger signal Again if lysis does not appear by the end of the third week the outlook becomes grave In our experience also the patient giving a positive blood culture late in the disease is suffering from an infection of more than usual severity The occurrence of hæmorrhage unless small in amount and not repeated should be regarded as of serious import and even if the patient rallies from the effect of the bleeding his resistance is bound to be weakened When perforation occurs the outlook is ominous as even the best operative results show a meagre survival rate In the typhoid state the outlook is most grave whilst meteorism and

be clearly explained that this is not a substitute for the most crupulous attention to surgical cleanliness in all dealings with the patient as it does nothing to protect her contacts The patient must be kept in bed in the recumbent position and under constant supervision during his whole illness The bed pan should always be used and in cases of severe exhaustion tow may be used to receive excreta Special care of the skin is necessary blanket bathing being performed twice daily followed by attention to pressure points In order to prevent bed sores and hypostatic pneumonia the patient s position in bed should be altered several times daily The mouth should be swabbed carefully with boroglycerine before and after feeds and much can be done to keep the mouth clean by ensuring that the patient drinks copiously between feeds The abdomen should be examined daily by the physician and the nurse instructed to save the stools for his inspection With regard to *diet* many systems have been devised but all are agreed that this is one of the most important aspects of treatment Milk is the best foundation and 3 pints per day equivalent to about 1 200 calories is a suitable amount for an adult patient to begin with This should be divided into two or three hourly feeds diluted with water or peptonised Should curds appear in the stools 1 gr of sodium citrate should be added to each ounce of milk and if undigested milk continues in the stools each feed should be reduced by half an ounce Such a diet should be given for a day or two until some indication can be obtained of the patient s ability to deal with nourishment Tentative additions in the shape of lactose or glucose cream strained oat flour porridge Bengers Ovaltine or others of the proprietary foods should then be made and even in severe cases are often well tolerated Some recommend a more liberal diet including meat extracts and beef tea bread and butter mashed potatoes and raw eggs beaten in milk from the very commencement of treatment but we are of the opinion that it is better to delay such additions until an estimate can be made as to how they are likely to be assimilated In our experience the main objection to a diet with milk as its chief basis is that many patients rapidly acquire a distaste for it but this may be overcome by giving the milk in the form of ice cream junket or milk jellies and flavouring with

or 0 5 1 0 and 1 5 c c at weekly intervals Febrile reactions and localised induration and redness not uncommonly follow these injections but protection is quickly developed and is estimated to last for one or two years For those likely to be exposed to enteric the method can be recommended as safe It was subjected to a severe test during the war of 1914–18 and according to Topley (1933) can be held to have established itself as a reliable protective measure for those exposed to serious but not overwhelming risk for a limited period of time A new type of typhoid paratyphoid vaccine containing the Vi antigen has been introduced by Felix Rainsford and Stokes (1941) with a view to securing more complete protection, and preliminary work with this indicates that reactions are less severe following injections Some discussion has arisen of recent years during large outbreaks in urban communities as to the advisability of actively immunising those who have been exposed to a common source of infection such as water or milk The well known experimental findings of a negative phase following injections of enteric vaccines deters many from recommending active immunisation to those who may be incubating the disease lest provocative typhoid ensues and on theoretical grounds the employment of the Felix antiserum with a view to producing passive immunisation ha been recommended The offic al view expressed by the Ministry of Health is that in the United Kingdom the question of active immunisation of individuals already exposed to infection does not arise until the necessity for it has passed but in this connection it is important to note from the experimental work of Schutze (1939) that in mice vaccination after infection does not damage the animals normal resistance but that in a considerable proportion of cases it actually enhances it

Treatment In this disease the most careful nursing and watchful attention on the part of the doctor is required The management of enteric patients should only be entrusted to experienced nurses who have been thoroughly trained in the principles of asepsis and if the proper ritual is carried out there need be no danger to the nurse or to others with whom she may be brought in contact As an additional precaution active immunisation may be offered to nurses but it should

beta naphthol and as Caiger recommended sulphurous acid or oil of cinnamon but bearing in mind the pathology of the condition it is doubtful if many would place much reliance on these nowadays Of the special methods we are biased towards the *antisepsis by elimination* treatment practised by Ker in which the objective is the prevention of stasis and intestinal putrefaction which encourage and complicate the ulcerative process This is secured by giving calomel in 3 grain doses every second or third day followed four hours after by an irrigation of 3 or 4 pints of water at 116 F Contra indications are meteorism and hæmorrhage and in severe cases in which the ulcerative process is likely to be well marked it is not advisable to persist with treatment beyond the first two weeks of illness The method is safe and in the mild cases of paratyphoid with which we are frequently confronted at the present time one or two treatments often have a striking effect In sharp contrast to the above Pugh (1937) has drawn attention to a method he had formerly practised Following the observation at operations that perforation and hæmorrhage resulted from intestinal distension and peristalsis his aim was to diminish these as far as possible by the local application of continuous cold to the abdomen a minimal residue diet of whey containing plasmon and lactose and the administration of starch and opium enemas or opium by the mouth He mentions that in this way more than one patient s bowels remained unopened for five weeks without ill effect and that cases which came under treatment moderately early showed satisfactory results The *cold-bath* treatment has been warmly recommended by many including Goodall and has been fairly widely employed in hospital the patient being given baths of ten to twenty minutes duration at a temperature of 80 –85 F every four hours Stimulants must be kept in readiness and warmed blankets and hot bottles prepared for the return of the patient to bed Treatment by *specific vaccines* of various types has been tried and in occasional cases has given spectacular results Since similar effects have been produced by the injection of *non specific substances* such as sterile milk peptone and normal horse serum it would appear that they are largely explicable on the basis of protein shock Many attempts have been made to obtain a *specific antiserum* but until recently

cocoa or coffee. Not infrequently the medical attendant's ingenuity may be severely taxed in devising a suitable diet for an enteric patient and probably the main point to appreciate is that any rigidly preconceived routine system of dieting is almost certain to break down when faced with the idiosyncrasies of the individual. *When the temperature has settled* in a severe case or at an earlier stage in milder forms of the disease the diet can be gradually increased by adding thoroughly cooked milk puddings, custard, lightly boiled egg and potatoes mashed with butter. Later pounded fish

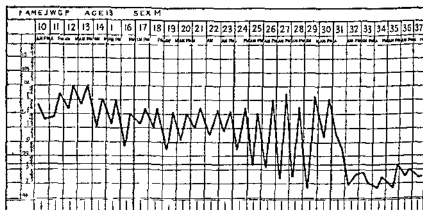


FIG 41. Temperature chart of sharp case of enteric fever. Note unusual mode of termination of fever on thirtieth and thirty first days of disease. Patient's general condition was very good from the twenty fourth day onward but the expected lysis was incomplete until the somewhat liberal diet was replaced by a strict milk diet for a few days commencing on the thirtieth day

tripe and chicken are given and so to a full diet. Care must be observed to avoid dietetic indiscretions during the period of intense hunger which accompanies or succeeds the period of lysis and even a carefully regulated diet if it be too liberal may retard lysis. If diarrhœa or meteorism appear milk should be boiled and lime water added whilst in some cases milk will have to be withdrawn and albumen water substituted for a day or two. In hæmorrhage it is advisable to stop the diet altogether for at least twenty four and preferably forty eight hours. Apart from dieting various systems of treatment have been recommended and in the past attempts have been made at *intestinal disinfection* by such substances as salol or

of value and if the pulse rate and heart sounds indicate heart failure brandy or champagne may be given with benefit but in alcoholics it is better to rely on injections of strychnine or coramine In slight *hæmorrhage* in addition to starvation several 10 gr doses of Dover s powder should be given by the mouth at four hourly intervals but in severe cases ¼ or ½ gr hypodermic injections of morphine should be administered immediately and repeated if necessary from time to time during the next twenty four or forty eight hours The foot of the bed should be raised and if the above measures are effective sips of water by the mouth or ice to suck should be all that is permitted to the patient for twenty four hours before a return is made to milk When the patient has lost much blood transfusion should be considered In *perforation* surgical aid should be sought at once The management of convalescence will depend entirely on the severity of the illness and there are great variations in the time taken by individual patients to regain their strength but in general the convalescent period is prolonged and should not be unduly hurried Before terminating precautions necessary to prevent spread of infection or before discharge from hospital two or three consecutive examinations of stools and urine at weekly intervals should have been negative for the presence of organisms of the enteric group

Treatment of Carriers These may come to light in the investigation of outbreaks or an attack of the disease may terminate in the carrier state repeated culture of the stools or urine or both disclosing the pathogen While many of these clear up under observation in hospital it has been our experience that persistent carriers will continue to yield positive stools or urine on weekly examination for months When this state of affairs exists after the patient is clinically well and would otherwise be ready for discharge from hospital attempts at clearing the tissues should be made by chemotherapy one or two courses of sulphanilamide sulphathiazole or sulphaguanidine being given On the basis of experimental work this measure is worth trying in both intestinal and urinary carriers In spite of the fact however that observations at operation at the City Hospital have established that sulphapyridine is excreted in quantity in bile aspirated from the common duct

without much success An antiserum prepared by the immunisation of horses with a typhoid antigen containing both O and Vi principles the later so named because it is claimed to be closely associated with the virulence of the organism has been introduced by Felix (1935) who has reported beneficial results in severe cases of the disease in Palestine The antiserum is given in 50 c c doses on three consecutive days intramuscularly or intravenously diminution of toxæmia being the chief effect noted a favourable effect on the temperature curve being found less often McSweeney (1935 and 1937) has also been impressed with the results of the antiserum, as have others but at present clinical opinions seem somewhat discordant and our own limited experience indicates that final proof awaits more extensive trial As was to be expected *chemotherapy* has been attempted in the treatment of enteric and Harries Swyer and Thompson (1939) have reported favourably on the use of sulphanilamide and also sulphapyridine in conjunction with the Felix antiserum in the treatment of typhosus infections On the basis of our own results however we have been unable to discern any noteworthy degree of benefit ascribable to these substances or to sulphaguanidine In the meantime therefore apart from dieting and special methods such as are outlined above treatment is largely symptomatic *Hyperpyrexia* is best treated by cold or tepid sponging four hourly or by the ice cradles *Headache* can usually be relieved by aspirin and phenacetin and cold applications to the head Chloral and bromide or paraldehyde should be given in *insomnia* if this is not relieved by sponging In *diarrhœa* if modifications of diet do not have the desired result Dover s powder and irrigation of the colon with hot water should be prescribed *Constipation* especially troublesome in convalescence can be relieved with liquid paraffin and at this stage of the disease we have found it necessary to administer liquid paraffin practically as a routine In *meteorism* turpentine enemata or oil of cinnamon given by the mouth may be tried whilst a flatus tube passed well into the rectum is sometimes useful In the more desperate cases we have tried pituitrin eserine and acetylcholine with but scant success When *toxæmia* is obvious continuous glucose saline by the drip method may be

we have had complete lack of success in the treatment of intestinal carriers by sulphonamide compounds Impressed by the favourable results of these substances in other urinary infections we have given them to enteric urinary carriers but except for one or two successes the results have been dis appointing Nor have any of the other intestinal or urinary antiseptics we have tried been more encouraging Should these methods prove ineffective then recourse must be made to surgical methods After what interval of time the patient should be regarded as a chronic carrier and the responsibility undertaken of recommending surgical intervention depends on circumstances Some would only regard an individual as a chronic carrier after the patient had continued to excrete the organisms for a year but we have usually found that patience is exhausted when recovery has been established for two or three months and the restrictions of hospital isolation have been prolonged for that period As a practical point it should be remembered that even small quantities of the urine of a urinary carrier mixing with the stool may lead to the classifica *tion of the patient as both a urinary and intestinal carrier* The necessary care should therefore be taken in collecting specimens to prevent this error

For the treatment of *intestinal carriers* removal of the gall bladder has been recommended by many including Browning and his co workers (1933) as holding out the most favourable prospect of terminating the carrier state As a preliminary to operation however the duodenal contents should be aspirated through the duodenal tube after a meal and subjected to bacteriological examination In the gall bladder carrier the organism will be invariably found X ray examination of the *gall bladder region should also be carried out as in a number* of chronic carriers there is a demonstrable lesion which gives weight to the recommendation for operation It is under standable that this is important to the patient as if it can be shown that there are other and weighty reasons why he should subject himself to operation apart from terminating the carrier state these may induce him to submit to an operation which he might otherwise be disinclined to undertake Even should X ray findings be negative operation should still however be recommended When advising operation it should be remem

bered that cholecystectomy is associated with a definite operational mortality and it is imperative to assess carefully the general condition of the patient and as Bigelow and Anderson (1933) have pointed out to confine operation to those who are good surgical risks Cholecystectomy can be relied on in all but a small percentage of cases to put an end to the intestinal carrier state and in our own experience we can recollect only one unsuccessful operation in which as bacteriological examination of the stools still showed the presence of enteric organisms after removal of the gall bladder it could only be concluded that infection had spread to the liver ducts Most of our cases have given one or two positive stool cultures immediately after operation but thereafter successive negatives have proved the success of the procedure

In the investigation of a *urinary carrier* separate specimens of urine should be obtained from each kidney by ureteral catheterisation for bacteriological examination because frequently the persistent focus is unilateral Pyelography should also be carried out as more than once we have found advanced pyelonephrosis which had hitherto escaped recognition and which was probably the underlying pathological condition perpetuating the carrier state Removal of the kidney in such cases has brought about prompt cure of the carrier state and at the same time rooted out a potential danger to the patient

Carriers refusing or unfitted for surgical treatment should be excluded from any occupation involving the manufacture or distribution of food or drink in any form and should be taught habits of personal hygiene in thorough detail The success attending these methods will obviously depend on the intelligence of the carrier and unfortunately in many instances this is of a low order Theoretically however it ought to be possible to train the more teachable individual so that he is no more a danger to the community than a nurse attending a case of enteric Working on these lines the New York City Health Department reports a considerable measure of success in its surveillance of carriers



FIG 4 Print showing renal calculus and chronic kidney destruction in female patient aged fifty two suffering from chronic carrier state after paratyphoid B fever The kidney condition was old standing and symptomless and only came to light on genito urinary examination when the carrier state after paratyphoid was being investigated Carrier state terminated by nephrectomy



Fig 43 Phenomenon of Deb[illegible] and Ravina [illegible]cited by int[illegible]a cutaneous [illegible]nject[illegible]on of 0[illegible] c c convalesc[illegible]nt measl[illegible]s serum forty-e[illegible]ght hours before appearance of erupt[illegible]on

CHAPTER VIII

MEASLES

Synonyms—Morbilli Rubeola—the latter term now having been largely abandoned

Pathology *Although claims were made by Caronia (1921)* by Tunnicliff and others (1926) and by Ferry and Fisher (1926) on behalf of various cocci as the etiological agent in measles in none of these was the work confirmed and most were inclined to accept the commonly held assumption that the disease was due to a virus Blake and Trask (1921) reported reproduction of the disease in monkeys and carried on the virus for *six generations* but *for a considerable period* little advance was achieved Stokes and his co workers (1942) however appear to have put the matter beyond doubt by transmitting measles to Macaca mulatto by the inoculation of body fluids obtained from children with active measles and also by propagating measles virus through large numbers of passages *in chick embryo The egg passage virus has induced* measles in both monkeys and in susceptible children

The only immunity test so far elicited is that of Debré and Ravina (1923) who found that convalescent measles serum when injected intradermally into a patient in the prodromal stage of measles before the eruption of the true rash produces an *area in which the oncoming rash is inhibited This* reaction is quite convincing but its interest is somewhat academic as it is valueless in diagnosis It supplies ocular proof however that convalescent measles serum definitely contains antibodies

No characteristic post mortem appearances have been *observed in the rare cases in which* the patient has succumbed in the early eruptive stage of the disease those found in the general run of cases coming to the post mortem table being ascribable to such complications as broncho pneumonia or cerebral complications following acute otitis media McCartney (1934) *has pointed out that the type of consolidation found after measles pneumonia* is of the interstitial variety often in conjunction with obliterative bronchiolitis

Etiology Measles is found among all races and climates and in the temperate zones of Europe the seasonal incidence is from December to May the peak occurring usually about March but occasional rises in prevalence may be found even in June It should be noted however that in hot countries such as Spain Portugal and Egypt the summits of the mortality curves appear regularly in the hot seasons Epidemics occur with great regularity in London and in other large urban communities every second year whilst in others from two to six years intervene between outbreaks The age incidence is chiefly in children and from the sixth month of life onwards measles becomes increasingly prevalent until the 4–5 age period when it reaches its maximum In England and Wales measles mortality has shown a well marked decline since 1916 but until the advent of the sulphonamides was still responsible for the death of more children in the first three years of life than any other infectious disease with the possible exception of whooping cough and in the decade ending 1935 on an average accounted for about 4 000 deaths per annum As the measles mortality was largely the result of broncho pneumonia a complication which yields to treatment by the sulphonamides in a high proportion of cases it has certainly undergone a significant reduction and it is possible that in the decade subsequent to 1935 it will no longer occupy the prominence as a fatal disease of children that it has done in the past The mortality is highest in the second year of life and rapidly diminishes after the fifth year males being subject to a higher death rate than females Mortality rates are higher in urban than rural communities this being due to the later age at which country children contract the disease and from the returns in England and Wales it is also found that measles mortality is higher in the northern counties than in the southern Since measles has not been generally notifiable until recently it is impossible to estimate case fatality rates with reasonable accuracy In isolated communities in which measles is infrequent or unknown and the inhabitants therefore unprotected by previous attack the disease when introduced affects all age groups classical examples of this having occurred in the Faroe Islands and Fiji outbreaks

Transmission The source of infection is a case in the pro

onset of the true eruption but occasionally this period is exceeded and characteristic prodromal signs have been observed for as long as seven or eight days The patient becomes dull and apathetic and the earliest sign may be a *flicker of temperature* of no more than a rise to 98 or 99 F from a normal axillary temperature of 97°–97 4 F Signs of *coryza* also appear early with sneezing running at the eyes and nose suffusion of the conjunctivæ or actual *conjunctivitis* some *enlargement of the tonsillar glands photophobia and cough* *Pyrexia* will be found usually at this stage also in some cases the temperature mounting steadily through the catarrhal period till the true rash comes out but on the other hand there may be a remission to normal for day or two prior to the rash *Laryngitis* is not infrequent and occasionally produces obstructive signs indistinguishable from those of laryngeal diphtheria while some degree of *enteritis* may also occur Both of these conditions tend to disappear when the true rash comes out From the diagnostic standpoint the most important sign at this stage is the appearance of *Koplik spots* These are pathognomonic and are minute whitish grey specks pin point in size rather like salt grains distributed on the buccal mucosa They appear two or three days before the true rash but we have noted them in a few cases for as long as a week beforehand At first few in number they are usually found opposite the lower molars and at this stage a surrounding red areola may be recognised Towards the efflorescence of the true rash they become abundant over the whole mucous surface of the cheeks lips and gums but the areolæ tend to fade The pale smooth character of the mucosa is lost and becomes reddened and dry The patient often complains of

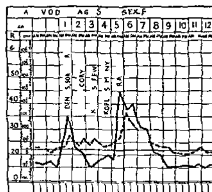


FIG 44 Temperature and respiration chart of a case of measles showing characteristic prodromal spiking followed by a pyrexial period and then pyrexia of eruptive stage

dromal or eruptive stage of the disease, the virus being contained in the nasopharyngeal secretions and disseminated by droplet infection *Away from the human host it shows little* or no vitality though it can probably be carried for short distances in the air *e g* within the confines of a ward, or on the hands or clothes of an intermediary There is no carrier state in measles

Infectivity As estimated by case to case infection this is of a high order measles in this respect resembling variola major and chickenpox so that when epidemics occur they are widespread and a high proportion of individuals unprotected by previous attack contract the disease at the first time of exposure For example Kelly and Reite (1934) have reported that about 50 per cent of family contacts succumb to exposure whilst Butler in London gave a figure of 66 1 per cent The period of maximum infectivity is during the prodromal stage of catarrah and whilst most authorities believe that infectivity does not outlast the rash current practice assumes that the patient remains infectious for about a week after its appearance There is no evidence that infectivity is prolonged by discharges, *e g* from the ear or by complications such as broncho pneumonia *One of the practical outcomes of the high infectivity* of measles is that in hospital ward outbreaks it is useless to attempt to circumscribe infection by other than cell isolation methods

Incubation and Quarantine Periods The incubation period is generally regarded as from 8 to 12 days if initial symptoms be regarded as the commencement of the disease or from 12 to 15 days if calculated to the appearance of the true eruption Whilst the great majority of cases conform to these times it should be kept in mind that in epidemics incubation periods of 21 days are by no means unknown Goodall (1931) has pointed this out and statistical work by Stocks (1931) supports his observations A quarantine period of 16 days is usually considered sufficient for exposed susceptibilities but we are in agreement with Goodall s recommendation of 21 days in ward outbreaks

Clinical Features **Stage of Invasion** This is also known as the *prodromal* or *catarrhal* stage and in the bulk of cases is quite well marked It lasts for three or four days before the

onset of the true eruption but occasionally this period is exceeded and characteristic prodromal signs have been observed for as long as seven or eight days The patient becomes dull and apathetic and the earliest sign may be a *flicker of temperature* of no more than a rise to 98 or 99 F from a normal axillary temperature of 97 -97 4 F Signs of *coryza* also appear early with sneezing running at the eyes and nose suffusion of the conjunctivæ or actual *conjunctivitis* some *enlargement of the tonsillar glands photophobia and cough* *Pyrexia* will be found usually at this stage also in some cases the temperature mounting steadily through the catarrhal period till the true rash comes out but on the other hand there may be a remission to normal for day or two prior to the rash *Laryngitis* is not infrequent and occasionally produces obstructive signs indistinguishable from those of laryngeal diphtheria while some degree of *enteritis* may also occur Both of

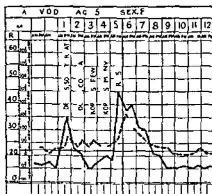


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Fig 45 Fully developed measles rash

sore throat and there may be well marked faucial angina with enlarged and angry tonsils The tongue is dry and furred stomatitis is often present and the teeth and gums coated with sordes In a proportion of cases this initial stage may be accompanied by the appearance of *prodromal rashes* Often they are patchy ill defined erythemata but sometimes they may simulate the rash of scarlet fever fairly closely and also that of the true rash of measles itself On occasion they are the first signs of the disease and occur five or six days before the true rash and before Koplik spots are seen or again they may be delayed until the day before the onset of the true rash

Stage of Eruption This is ushered in by the appearance of the true rash which comes out behind the ears and over the brow and in from twelve to twenty four hours it spreads over the whole of the face trunk and limbs In character at first macular it rapidly becomes papular dusky in colour and the lesions running together give a blotchy appearance any intervening skin uncovered by the rash retaining its natural appearance Sometimes the rash is confluent especially on the face and body and again certain of the rashes are decidedly hæmorrhagic in type This indeed is more or less characteristic of all measles rashes but may only become evident when the rash begins to fade and does not denote a hæmorrhagic or toxic type of the disease as in other eruptive fevers During the evolution of the rash the temperature rises to 102 -103 F and the patient is most miserable His face is blotchy and swollen the eyes and nose running there is a frequent harsh painful unproductive cough and he is restless and not infrequently delirious The respiratory tract is early involved respirations are quickened to 30 or 50 per minute and an acute bronchitis is present frequently before the rash comes out

Stage of Defervescence and Convalescence Once the rash is completely out the temperature begins to fall and in uncomplicated cases comes down by crisis in from twenty four to forty eight hours With defervescence the rash fades from above downwards the respiration rate is reduced and the general condition improves The cough becomes looser the appetite returns and in the course of a week or ten days the

patient is practically back to normal After the rash fades it leaves a brown staining which persists for varying periods and in cases in which it has obviously been hæmorrhagic the rash is succeeded by purplish staining which may take weeks to disappear thus enabling a retrospective diagnosis to be made during that period A branny desquamation involving the whole of the rash area simultaneously often succeeds the rash especially if this has been heavy Desquamation may also occur on the tongue giving an appearance not remotely resembling the clean tongue of scarlet fever but leaving a rougher surface

Complications These are of the greatest importance in measles a fatal result being very frequently due to respiratory complications Furthermore the late results of measles may produce invalidity from chronic chest conditions impaired vision or even blindness following eye complication or deafness and persistent ear discharge due to chronic otitis media

Laryngitis As already noted this may be seen in the pro dromal stage and whilst this variety occasionally disappears during the eruptive stage it may continue and be associated with broncho pneumonia In extreme cases if it persists œdema and ulceration of the larynx give rise to well marked obstructive signs A laryngitis occurring in convalescence is frequently diphtheritic in nature and should be treated as such at the first signs of hoarseness

Bronchitis This is present to some extent in every case and may persist for a few days when the rash has faded thus delaying resolution of temperature and convalescence

Broncho pneumonia is the most important and fatal of measles complications and indeed it is doubtful if strictly speaking it should be regarded as an actual complication but rather as an integral part of the disease Although the predominant role is usually assigned to the streptococcus as the secondary invader in measles the pneumococcus is by no means unusual The younger the child the more likely is it to be the subject of broncho pneumonia and whilst the investi gations of Kohn and Koriansky (1929) have disclosed radio logical evidence of the presence of the condition in a high proportion of cases before or during the height of the eruption

opacity may result and on occasion the process may result in perforation into the anterior chamber and panophthalmitis

Otitis media is one of the common complications of measles and in hospital practice is found in about 10 per cent of cases It appears usually in convalescence the onset as a rule being more acute than in scarlet fever and accompanied by pyrexia and pain followed by perforation Mastoiditis tends also to be more acute in its manifestations than in scarlet fever and in some cases the inflammatory process spreads with great rapidity to neighbouring structures with extensive bone destruction and leading quickly to lateral sinus thrombosis cerebral abscess or streptococcal meningitis

Adenitis of the cervical lymph glands is not infrequent The glands become enlarged and indurated there is some irregular pyrexia and suppuration may occur

Enteritis This may appear at any stage in the disease and in hospital and institutional outbreaks unless meticulous care is taken in applying aseptic methods of nursing is prone to spread rapidly among weakly and under nourished children It commences with frequent small loose motions green in colour and offensive Later mucus blood and even sloughs appear in the stools and the patient rapidly wastes The condition is often resistant to treatment dragging on for a week or two and death from this complication makes a definite contribution to the measles mortality In spite of the clinical resemblance to bacillary dysentery which many of these cases assume in our experience bacteriological investigation has failed to disclose the presence of the specific organisms of this condition in all but a few cases

Encephalitis Much attention has been drawn to this condition in recent years although numerically cases are relatively rare Clinically and pathologically it cannot be distinguished from the encephalitis found in association with others of the acute infections but it has probably been more frequently reported after measles than others It appears usually between the third and tenth day after the rash and is manifested by pyrexia increasing drowsiness or stupor or irritability and delirium convulsions signs of meningeal irritation general muscular rigidity cranial nerve palsies and incontinence Lumbar puncture reveals a clear or slightly

definite clinical diagnosis is seldom possible until the rash fades After that the continuing pyrexia and well marked signs are unmistakable The patient is restless and cyanosed respirations are rapid laboured and grunting and in severe cases there may be some recession of the lower intercostal spaces Patches of consolidation and abundant crepitations are noted and when the condition persists exhaustion becomes extreme and death occurs in many cases about the end of the third week from heart failure convulsions also occasionally being a terminal feature Pleural effusion and empyema occur in a fair number of cases and when it does the outlook becomes very

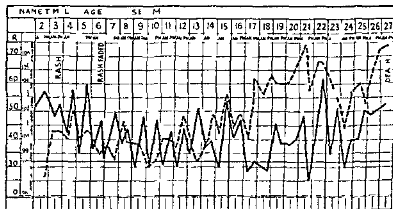


Fig 46 Temperature and respiration chart of fatal case of measles broncho pneumonia

grave indeed Even should apparent immediate recovery ensue, chronic fibroid and bronchiectatic changes may leave a legacy of prolonged pulmonary damage especially in those as Westwater (1934) has pointed out who have suffered from respiratory disease prior to the onset of measles Whilst in the past some have associated these chronic changes with tuberculosis this view does not now find favour An attack of measles may terminate fatally however in tuberculous broncho pneumonia

Eye Complications Nearly all cases suffer to some extent from conjunctivitis and blepharitis which appear during the pre eruptive and eruptive stages Unless conscientious treatment is carried out ulceration of the cornea with subsequent

opacity may result and on occasion the process may result in perforation into the anterior chamber and panophthalmitis

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hazy fluid under increased pressure with some increase in the mononuclears The fluid is sterile shows a slight or moderate increase in protein normal or increased sugar and normal or slightly decreased chlorides After several days the condition gradually improves in the majority but from 10 to 30 per cent of cases are fatal and residual palsies mental deterioration and Parkinsonism have been reported

Other Complications Ulcerative stomatitis may give a good deal of trouble especially when broncho pneumonia is also a complication Cancrum oris a condition little seen nowadays used to be relatively common in measles and indeed was said to be associated with measles more frequently than any other infectious disease

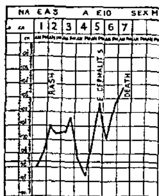


FIG 47 Temperature chart of rapidly fatal case of post measles encephaliti

Associated Diseases Measles may be found in conjunction with *any of the infectious diseases* but particularly with whooping cough and diphtheria When measles and whooping cough co-exist the effect is serious owing to the ever present risk of broncho pneumonia When diphtheria occurs in conjunction with measles it is liable to be of the laryngeal type and any case of croup appearing in the eruptive or convalescent stages of measles should be promptly treated as diphtheritic *Scarlet fever whilst perhaps less* frequently found in association with measles is an unfortunate complication otitis media being particularly likely to occur

Relapse and second attack are practically unknown one attack almost invariably conferring life long immunity

Varieties of Measles Generally speaking measles reveals itself as a well developed clinical entity and the great majority of cases conform to the average type described above *Mild types* however are common especially in older children and in these all the signs and symptoms are mitigated the prodromal stage is brief and mild in its manifestation the eruptive stage is short and the rash though quite definitely developed

is not very intense and fades early Pyrexia and respiratory symptoms are slight and the disease runs its course in two or three days without complications Also a mild type may occur in which catarrh is practically absent Lastly a child may show a characteristic prodromal stage which is followed by a scanty rash or even no rash at all *Severe or malignant types* are rare and include a *hæmorrhagic type* in which bleeding occurs from all mucous surfaces and into the skin and a *toxic* type with high fever delirium great prostration and a poorly developed rash ending fatally in one or two days A very rare bullous type of measles has also been described and although some have disputed the existence of *morbilli bullosi* nevertheless well authenticated cases of measles with a rash showing pemphigoid elements have been reported James and Miller (1938) have described a fatal case and one coming under our own observation was successively covered from the face and neck downwards with bullæ of varying sizes containing amber coloured fluid death occurring in forty-eight hours after the appearance of the rash Ronaldson (1937) is of the opinion that the term morbilli bullosi should be reserved for a bullous variety of the measles eruption and cannot properly be applied to a type of the disease It should also be observed that most of those with a considerable experience of fevers have occasionally seen cases with an intense dusky morbilliform rash followed immediately by a widespread bullous eruption and profound toxæmia in which there is a temptation to make a diagnosis of morbilli bullosi The absence of epidemiological relationships with other cases of measles and such clinical features as catarrhal onset and Koplik spot should engender caution and most fever clinicians are content to classify these as acute pemphigus whilst some dermatologists prefer to regard them as forms of dermatitis

Diagnosis In the prodromal stage the only certain sign is the Koplik spot but since that is usually preceded by catarrh the exposed susceptible should be isolated under observation at the first sign of this or if the temperature shows the slightest disposition to rise above the true average level Furthermore *suspicion should not be allayed if a remission of temperature* occurs after a day or so In differential diagnosis the occurrence of laryngitis at this stage may lead to the conclusion that the

hazy fluid under increased pressure with some increase in the mononuclears. The fluid is sterile, shows a slight or moderate increase in protein, normal or increased sugar, and normal or slightly decreased chlorides. After several days the condition gradually improves in the majority, but from 10 to 30 per cent. of cases are fatal, and residual palsies, mental deterioration and Parkinsonism have been reported.

Other Complications. Ulcerative stomatitis may give a good deal of trouble, especially when broncho-pneumonia is also a complication. Cancrum oris, a condition little seen nowadays, used to be relatively common in measles and indeed was said to be associated with measles more frequently than any other infectious disease.

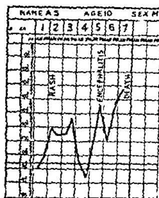


Fig. 47. Temperature chart of rapidly fatal case of post-measles encephalitis.

Associated Diseases. Measles may be found in conjunction with any of the infectious diseases, but particularly with whooping-cough and diphtheria. When measles and whooping-cough co-exist the effect is serious owing to the ever-present risk of broncho-pneumonia. When diphtheria occurs in conjunction with measles it is liable to be of the laryngeal type, and any case of croup appearing in the eruptive or convalescent stages of measles should be promptly treated as diphtheritic. Scarlet fever, whilst perhaps less frequently found in association with measles, is an unfortunate complication, otitis media being particularly likely to occur.

Relapse and second attack are practically unknown, one attack almost invariably conferring life-long immunity.

Varieties of Measles. Generally speaking, measles reveals itself as a well developed clinical entity, and the great majority of cases conform to the average type described above. *Mild types*, however, are common, especially in older children, and in these all the signs and symptoms are mitigated: the prodromal stage is brief and mild in its manifestation, the eruptive stage is short, and the rash, though quite definitely developed

Prognosis Although measles is a comparatively uneventful incident in the lives of the great majority of children it should not be regarded as a trivial disease in those under five and its special severity in those under two should be remembered Evidence of malnutrition constitutional disease such as rickets previous chest ailments or susceptibility to naso pharyngeal infections should enjoin caution in prognosis It is rare for a fatal result to occur in the eruptive stage but the failure of respiratory signs to improve fairly soon after the fading of the rash makes the position anxious since broncho pneumonia is the great danger in measles in the past this complication showing fatality rates of 20 to 50 per cent It is to be noted however that since the advent of the sul phonamide drugs the prognosis in measles bronchopneumonia has undergone a substantial improvement with the result that hospital mortalities have shown a considerable reduction For example at the Edinburgh City Hospital between 1928 and 1938 inclusive the overall measles fatality in 4 069 cases was 7 68 per cent whereas between 1939 and 1944 inclusive in 1 757 cases it was 1 65 per cent It is not suggested that these figures give a true picture of the general measles fatality in all cases as many patients are admitted to hospital on account of the severity of their attack but they do emphasise the remarkably improved prospects which have followed the use of such drugs as sulphapyridine and sulph thiazole In individual cases of measles bronchopneumonia those with no previous history of respiratory disease or in whom signs of defective nutrition are absent do best Whilst the pulse is an excellent guide to prognosis the fairly rapid fall in tempera ture respiration rate and amelioration of distressed breathing within a day or two of the beginning of chemotherapy indicates a favourable prognosis even if the improvement in chest signs lags If the temper ture and pulse rate remain elevated if dyspnœa and restles ness persist and particularly if these signs continue for ten days or a fortnight the outlook is ominous Cases of laryngitis with obstructive signs sufficiently severe as to require operation show a high mortality and laryngeal diphtheria in the course of the disease carries a worse prognosis than in purely diphtheritic infections owing to the poor results of operative treatment A serious view

condition is diphtheritic and if obstructive signs are present diphtheria antitoxin should be given at once Scarlatiniform prodromal rashes may also cause difficulty especially if these occur before Koplik spots have appeared The problem is further complicated by the fact that scarlet fever and measles may be concurrent and the only course open may be to assume that both diseases are present until further observation enables a decision to be made In the stage of eruption the remains of Koplik spots the rash and the bleary appearance of the patient is sufficient to make a diagnosis Probably in measles as we see it at present atypical and abortive forms are much less common than in other exanthemata and the diagnosis is easy in the great majority of cases Differential diagnosis at this stage is concerned chiefly with the other exanthemata of which *rubella* probably resembles a mild attack of measles most closely In rubella the rash tends to remain discreetly macular or if it becomes confluent on the trunk it more closely resembles scarlet fever than measles Catarrh and suffusion of the conjunctivæ are common to both rubella and measles but Koplik spots are absent in rubella while in the latter the generalised shotty enlargement of the lymph nodes is usually to be made out The measles rash may also require to be distinguished from the *prodromal morbilliform rash of smallpox* which though measly in appearance is said not to be raised above the skin The *papular stage of smallpox* differs from measles in that in the former the distribution of the rash is centrifugal there is no tendency to blotchiness whilst shottiness of the papules may be made out whereas in measles catarrh is prominent and Koplik spots usually retrogressive during the eruptive stage often can still be identified during the first two days of the rash *Syphilitic* rashes may be mistaken for measles rashes but these are associated with a generalised adenitis *Teething* rashes in infants *food serum* and *septic* rashes including those seen in the septic type of scarlet fever may also produce some points of resemblance to the measles eruption One of the results of the employment of *sulphonamides* especially sulphapyridine has been that morbilliform rashes almost indistinguishable from those of measles have come under our notice as one of the toxic effects produced by these drugs

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should be taken of enteritis in infants and young children and the same applies to corneal ulceration As a rule the prognosis is good in middle ear disease if careful treatment is applied at the outset but occasionally spread to the mastoid and related structures is so rapid and acute that the situation is precarious from the beginning Once encephalitis has declared itself the prognosis should be very guarded and the patient who shows a steep uprise of temperature with early onset of coma rarely survives Moreover in those who recover post encephalitic phenomena with all their depressing changes in mind and body must be kept in mind So far we have only considered immediate prognosis but in addition the more remote outlook may be clouded by the occurrence of complications producing chronic chest troubles defects in vision and deafness It is well therefore to bear in mind that certain patients recovered from bronchopneumonia may need supervision for some years In modern times the specific fevers are comparatively unimportant causes of blindness according to Marshall and Seiler (1942) who have made a study of this defect in Glasgow and neighbourhood but of the small amount due to these measles was responsible for nearly three quarters of the total The position as regards deafness is more disturbing Kerridge (1937) having found among children attending special schools for the deaf in London that in those in whom the onset of otitis media could be traced to a specific fever 37 per cent followed measles When we consider the relatively high incidence of acute otitis media in measles the total amount of chronic ear disease and disability attributable to this infection throughout the country cannot be small There is no doubt that much can be done to prevent eye and ear defects by careful management in the acute stage of the disease and remote prognosis in respect of these would appear to depend therefore on the energy with which this has been provided at the outset

Prophylaxis In the past the decision as to making measles notifiable was left to local authorities who usually adopted a modified system applying to first cases in a family and from this and the school returns of absentees the medical officer of health obtained information on which to base administrative action As a measure of prevention of spread general notifica

tion followed by the usual measures of disinfection and isolation cannot be regarded as of much value in measles epidemics in which great numbers of children are simultaneously stricken but it is interesting to note that in 1939 regulations for the notification of all cases of measles were applied in England and Wales General administrative measures are directed towards limiting as far as possible the serious results of infection In the first place warnings to the general public should be issued as to the injurious consequences of measles in young children as to seeking medical aid when the disease occurs and against the wilful exposure of young children to those suffering from measles Practitioners should be informed as to the facilities for dealing with outbreaks and how they may be made use of Such facilities include home visitation by nurses who advise and assist with the management of patients and the provision of hospital accommodation for severe and complicated cases and for those in poor and over crowded home conditions While it has been generally accepted as a beneficial provision the policy of hospitalisaton on a large scale in the ordinary open ward of a fever hospital has been adversely criticised by some as tending to increase complications especially bronchopneumonia If strict regard is paid to adequate staffing free ventilation adequate floor space and particularly the maintenance of a proper distance between bed centres which in our opinion should be 12 feet it is difficult to believe that patients treated under such conditions will not do better than in the poor circumstances in which many would pass through their illness if left in their homes The investigations of Wright Cruickshank and Gunn (1944) indicate further refinements in ward management which would go far to meet the objections of those who condemn large scale hospitalisation of measles patients By introducing oil treatment of floors clothes and bedclothes they were able to reduce considerably though not to eliminate dust born streptococcal infections The method is not without drawbacks and for some time to come may not be generally applicable but at least it serves to emphasise the importance of dust control and the necessity for continuous study of all the minutiae which collectively make up the daily ward routine so that the transfer of infection from patient to patient may be avoided School

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sterile containers ready for use To obtain consistent results the serum from several donors should be pooled and until recently the reagent when produced with these safeguards has been regarded as absolutely safe and free from undesirable sequelæ It requires to be stated however that following the administration of injections of a single batch of convalescent measles serum in 1937 a series of cases of acute infective jaundice some of which proved fatal occurred in England Findlay MacCallum and Murgatroyd (1939) suggested that a virus had been introduced along with the serum and Cullinan (1939) recommends that pools of apparently normal human serum should not be used for human inoculation unless the medical history of all the donors can be followed for at least six weeks and that the donors should have had no history of jaundice in the past With regard to its employment various doses have been recommended but generally the practice has been to give 5 c c to children under three years and from 6 to 10 c c to those over three In our own practice however we have given a standard injection of 5 c c to all patients irrespective of age in whom protection is desired and the results have been highly satisfactory To secure complete protection serum must be given as early as possible in the period of exposure If given later than the fifth day it is currently stated that the disease will not be prevented but if given between that time and the eighth day a modified form of measles will result assuming that infection has taken place When given later than the eighth day it is doubtful if any effect is produced and attempts at serum therapy have largely been abandoned From the above it will be seen that in administering convalescent measles serum two objectives are possible *complete protection* or *modification* of the disease When complete protection is obtained the passive immunity so conferred is short lived on an average possibly not more than four weeks and while this may be of considerable value in hospital and institutional practice the fact that during epidemic periods children can hardly hope to avoid repeated exposure has led to the practice of intentionally delaying administration of serum until between the fifth and seventh day the object being to secure a modified attack harmless in itself but which will give an active immunity and which will be permanent

exclusion of susceptible contacts for twenty one days is also carried out in some areas but many including Forbes (1936) are of the opinion that this is useless in preventing spread in infected schools and that it is preferable for contacts to remain at school where they can be under supervision

Passive Immunisation Although Stokes and his co workers have shown that measles virus cultured in the chick embryo is so modified that an attenuated attack is produced when it is injected into susceptible children and that natural infection transmitted from these artificially induced attacks retains the characteristic mildness of the latter the great possibilities in active immunisation so opened up by these discoveries must await further investigation before practical use can be made of them In the meantime therefore we must continue to rely on passive immunisation which is based on the assumption that since measles results in a solid and permanent immunity *immediately after recovery the blood is rich in antibodies* which though subject to diminution with advancing years remain in appreciable quantity throughout life Advantage was taken of this fact by Nicolle and Conseil (1918) who introduced the method of injecting *serum from convalescent measles patients* into exposed susceptibles in order to produce a temporary passive immunity The efficacy of this method has been confirmed by numerous observers throughout the world and many public health authorities now seek to make use of it as far as their resources permit With the limited amount of serum available however it would be impracticable to attempt to protect all contacts It is generally agreed therefore that serum should be reserved for hospital or institutional outbreaks for the protection of children under five years and especially for those under three and for delicate children such as those suffering from chest or other constitutional diseases in whom the occurrence of measles might be dangerous Blood is withdrawn from measles convalescents seven to ten days after defervescence adult donors being able to give 100 to 300 c c without the slightest ill effect To avoid lipæmia the blood should be taken just before a meal the apparatus described by McCartney (1933) being very suitable In the laboratory the serum is separated Wassermann tested preservative is added and filled out in

into the recipient by the intramuscular route The question of blood grouping does not arise and the dosage is double that for the corresponding serum viz 10–20 c c of con valescent blood or 20–40 c c of adult blood the time of inoculation being varied according to whether complete protection or attenuation is desired It should be realised that after such injections a hæmatoma will be formed which will take some time to be absorbed A further development in measles prophylaxis has been reached by the introduction of *placental extract* by McKhann and his co workers (1933) This reagent consists of globulin obtained by extraction from the human placenta and Levitas (1935) reported successful results in protection and in attenuation Our own experience indicates that dose for dose it is probably only a little less efficacious than convalescent serum Reactions in children are trifling being confined to a short lived spike of temperature the day following injection and since further experience seems to confirm the reliability of the substance passive immunisation in measles will probably enjoy much wider application as the source of supply of the reagent is independent of the difficulties associated with the collection of human serum In the meantime we recommend an injection of 5 c c the exposure injection interval being varied as in convalescent measles serum according to whether complete protection or attenuation is desired Since the antibody content is less bulk for bulk than in convalescent serum the percentage of complete protections will be less and the proportion of modified cases greater Compared with adult immune serum placental extract is superior in effectiveness and appears to occupy a position midway between that reagent and convalescent measles serum Still another reagent *gamma globulin* for the production of passive immunisation in measles falls to be mentioned although it has not been much employed in Great Britain In the process of fractionation of pooled human serum developed for the production of normal human serum albumin by Cohn and his co workers this substance became available and was found to contain a variety of antibodies in high concentration Among these is measles antibody and gamma globulin has been used with success in passive immuni sation in the United States Stokes Maris and Cellis (1944)

This method originally suggested by Debre and Ravina (1923) is usually referred to as as sero attenuation but from our own observations in a series of wards outbreaks in which the exposure could be definitely restricted to a duration of twelve or twenty four hours it has been found that serum given on the sixth day of exposure will give complete protection to a respectably large proportion of cases and therefore if it is definitely desired to induce sero attenuation, it would be wise to delay serum until the seventh or eighth day As it is often difficult to establish the exact day on which any given case first became infective and since exposed susceptibles *e g* family or ward contacts have usually had opportunities to become infected over several days the intentional production of sero attenuation must always remain a somewhat uncertain undertaking The difficulty in maintaining an adequate supply of convalescent measles serum has led to the use of *adult measles serum* which is obtained preferably from young adults who have a previous history of measles and whose history is also satisfactory in respect of jaundice It is prepared in the same manner as the convalescent serum and it can generally be relied upon to secure attenuation but its value in producing complete protection is less certain The dosage is from 10 to 20 c c injected intramuscularly and to give complete pro *tection* Russell (1933) *advises that it should be administered* within three days of exposure especially in those under three years of age although in older children this provision is not so essential If attenuation is aimed at 10–20 c c should be given after the sixth day but Russell states that there is no necessity to defer inoculation as long as this since results equally good can be obtained by injections of half doses in the first three days of exposure with resulting economy of serum Where laboratory facilities are not available the use of *con valescent* or *adult whole blood* would appear to be the most practicable procedure for the practitioner The donor in the case of convalescent blood would generally be another member of the family and in the case of adult blood either or both the parents at least one of whom is almost certain to have a history of measles The blood should be drawn off into a record syringe containing 2 5 per cent sodium citrate in the proportion of 1 part citrate to 10 parts of blood and immediately injected



Fig. 49. Rash of case of attenuated measles at height of eruption. Note scattered discrete macules.

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recommending a dosage of 0 25–0 5 c c for attenuation and 2 0–2 5 c c for protection in children of five years and under and 1 0–1 5 c c for attenuation and 4 0–5 0 c c for protection in those aged six to twelve years Janeway (1944) states that gamma globulin in a dose of 0 1–0 075 c c per pound of body weight will protect most susceptibles while one of 0 025–0 02 c c will usually result in mild measles The advantages claimed for this prophylactic are that a small dose is required there is little or no discomfort at the site of injection and local and general reactions are rare

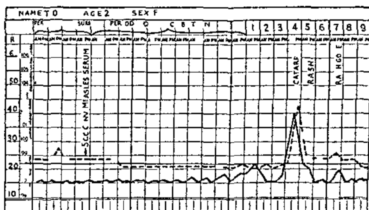


Fig 48 Temperature and respiration chart of case of attenuated measles Rash scanty and confined to chest and back Koplik spots absent Toxæmia slight Catarrh quite well marked No complications

Modified or attenuated Measles Clinically this form of the disease is represented by the very mildest manifestations The incubation period whilst occasionally prolonged to eighteen or twenty-one days does not as a rule last beyond the average limits The catarrhal stage may only be represented by slight lachrymation while Koplik spots are absent or sparse We agree with Gunn (1933) that typically the rash is the last clinical feature to be suppressed but its form is very different from that of the average measles case It is frequently confined to the face and the upper part of the trunk and consists of a scanty discrete or only slightly confluent maculo papular eruption lasting for one or two days Pyrexia may be absent or represented by a spike of temperature

lasting for twenty four or forty-eight hours respiratory signs apart from slight cough are absent the patient retains his alertness throughout and constitutional disturbances are negligible The infectivity of the attenuated case is low but there is no doubt that transmission can and does occur the resulting infection being unmodified

Treatment No specific treatment is available and the patient should be isolated in a room in which thorough ventilation is possible and indeed conditions should approximate to those of the open air as nearly as possible precautions being taken to maintain body warmth and to avoid bitter winds Light but warm bed clothes should be worn but some recommend a gamgee jacket and rubbing the chest with stimulating oils In the febrile stage milk diet should be prescribed and abundant drinking of water encouraged When the temperature has fallen the patient is advanced through light diet to full diet as soon as convalescence is established although in children the possibility of too rapid additions to the menu setting up gastro intestinal disturbances should be kept in mind Efforts have been made by the systematic administration of the sulphonamides in the early part of the illness to reduce the incidence of complications but the results of the work so far reported are somewhat inconclusive though both T Anderson (1939) and Hogarth (1939) report some diminution in otitis media In view however of the part played by the streptococcus in measles complications it might be considered useful to give sulphanilamide during the first week or ten days If there is *photophobia* a simple eye shade should be worn and *routine treatment of the eyes* should be commenced at the onset of all cases of measles by frequent irrigations with boric lotion If *conjunctivitis* is present half or quarter strength golden ointment should be applied to the inner surfaces and margins of the eyelids *Cough* will require a sedative mixture and the temperature may be kept within reasonable limits by tepid sponging Should the rash be slow in developing or bluish in colour hot bottles and blankets or hot packs may be necessary *Delirium* and restlessness may require sedatives such as chloral and bromide *Laryngitis* often improves with steam hot fomentations to the neck and anti spasmodic drugs and diphtheria antitoxin should be given at once

puration occurs incision and drainage is necessary *Enteritis* should be met by the immediate reduction of the diet to glucose albumen water or boiled milk to which lime water or citrate is added one or two small doses of grey powder and washing out the large bowel with saline or eusol is sometimes effective When dehydration occurs subcutaneous or intra peritoneal salines should be administered and it is wise not to postpone these measures until dehydration is extreme If intravenous injection is possible 5 per cent glucose in normal saline given by the drip method is of great advantage *Encephalitis* seem to benefit from lumbar puncture repeated if necessary and Mitman (1937) has reported a striking result following the intraspinal injection of serum derived from a measles patient recovered from this complication

Isolation From the point of view of infectivity isolation for two weeks from the appearance of the rash is ample but in hospital practice many cases are not fit to be discharged from the clinical point of view in less than three weeks *Otorrhœa* need not be an indication for the prolongation of isolation as in scarlet fever Cases convalescent from broncho pneumonia require a long period of recuperation preferably in the country and if facilities are available admission to an open air school should be sought

particularly if signs of obstruction are present Operative interference should be postponed as long as possible and tracheotomy is to be preferred to intubation as the irritated and sometimes ulcerated larynx will not tolerate the intubation tube In *bronchopneumonia* the patient should be placed near an open window and supported with pillows in a semi upright position Frequent nourishing feeds should be given and linseed poultices or cataplasma kaolin applied to the chest Treatment by one of the sulphonamide drugs should be commenced at once sulphathiazole being very suitable and as children tolerate them well a total dosage of 3 to 5 grms daily should be given for the first two or three days In the majority of cases a beneficial effect is obtained in the first forty eight hours in the shape of a fall in temperature and pulse rate and a diminution in dyspnœa The total daily amount may then be reduced to a maintenance dosage for the remainder of a seven day course Oxygen given by the nasal catheter may be of some benefit and should be given early but if the full benefits of oxygen therapy are to be realised the oxygen tent should be employed Whilst the results obtained by the oxygen tent were occasionally spectacular in measles bronchopneumonia in the pre sulphonamide era in general the effects were not so good as in the corresponding complications of whooping cough and at present it is on the sulphonamides that we must mainly rely for success in treatment Stimulants such as strychnine may be administered and we are of the opinion that frequent small doses of brandy 20 or 30 minims in hot water are valuable If pleural effusion appears repeated aspiration should be carried out with replacement by 10 000–20 000 units of penicillin Later if the exudate becomes purulent surgical drainage may be required For established *conjunctivitis* in addition to the routine treatment outlined for measles eyes frequent irrigation with 10 per cent albucid lotion may be employed If corneal ulcer appears the edges should be carefully carbolised and the pupil moderately dilated with atropine In *acute otitis media* if there is warning of the onset or at the first signs of otitis treatment by penicillin should be commenced at once The same remedy is called for when signs of *mastoiditis* appear *Adenitis* is treated by sulphanilamide and kaolin or linseed poultices and if sup

is air borne for limited distances e g within the confines of a ward The infective agent enters the body by inhalation

Infectivity Chickenpox is very highly infectious in this respect resembling measles and smallpox and Kelly and Reite (1934) give the secondary attack rate per 100 susceptible family contacts as 98 8 There seems little doubt that there is some variation in infectivity as between one case and another but it has been our experience in ward outbreaks that instances in which secondary cases do not occur are rare Moreover the highly infectious nature of chickenpox is shown by the fact that the barrier nursing methods applicable to some infections are quite useless in this disease which requires chamber nursing in its most complete form It has been held that the power to infect is practically synchronous with the appearance of the rash and we may agree with Gordon and Meader (1929) that the disease is infectious in the great majority of cases for only a short period preceding the eruption probably less than twenty four hours The duration of infectivity has been laid down by F H Thomson (1924) as not outlasting the end of the first week of the eruption or the beginning of the second and this has been amply confirmed in our own experience by the fact that we have never seen chickenpox occur in susceptibles exposed to cases after the tenth day of their eruption even though extensive scabbing was present

Incubation and Quarantine Period The incubation period is usually given as from 12 to 21 days outside limits being from 11 to 23 It is usually fairly constant and the findings of Gordon and Meader that in a high proportion of cases it fell within 13 to 17 days the commonest being 15 are in agreement with average experience A quarantine period of 21 days is therefore sufficient for all practical purposes

Clinical Features **Stage of Invasion** In the majority of cases the first sign of the disease is the appearance of the eruption but a certain number show a period of invasion which commonly lasts for two or three days and in exceptional cases for about a week During this time the patient may show malaise drowsiness loss of appetite headache vague pains and even some pyrexia The most important feature of this stage however is the occurrence of *prodromal rashes*

CHAPTER IX

CHICKENPOX

Synonym—Varicella

Pathology The observations by Aragao (1911) and Paschen (1919) of minute bodies in the lesions of chickenpox which were thought to be the actual infective agents of the disease have been confirmed by Amies (1933) Elementary bodies have been demonstrated by the last mentioned in vesicle fluid by staining methods and he has prepared from them purified suspensions which are specifically agglutinated by the serum of patients convalescent from chickenpox The findings that elementary bodies are constantly present in early vesicle fluid and their specific agglutination with homologus anti serum, he regards as strong evidence that they are the causal organisms After entrance into the body the virus is spread by the blood stream and the findings in a post mortem examination performed by Johnson (1940) in a child dying at the height of an attack of chickenpox from another cause would indicate that lesions similar to those found on the skin and visible mucous membranes are widely distributed In the case mentioned they were found in the œsophagus pancreas liver kidney pelvis adrenals ureters and bladder

Etiology The disease is found in all countries throughout the world and shows no particular sex or seasonal incidence It occurs chiefly in the first ten years of life but adults unprotected by previous attack readily contract the disease and we have seen chickenpox in two female patients aged eighty two and eighty nine years

Transmission The source of infection is a case of the disease spread being mainly by *droplet infection* and direct contact with the patient Infection may also be carried by an intermediary within short periods after contact of the latter with an infectious case whilst the studies of F H Thomson (1916) of hospital outbreaks in which contact infection was eliminated by barrier nursing have indicated that the disease



FIG 50 Ch kenpox e upt on showing l ons in p istu lar st ge w th c ntral s al b ng Many re rough ly oval n h pe w th irregular outl ne

The scarlatiniform type of these is relatively common and they may resemble the rash of scarlet fever closely in character and distribution Other prodromal rashes morbilliform urticarial and purpuric have also been described but in our experience are rare an ill defined patchy erythema being the only other initial rash commonly seen apart from the scarlatiniform variety The rash may appear a day or two before the true eruption or practically simultaneously with it In some cases it fades with the emergence of the pocks and in others it remains for some time after these have come out

Stage of Eruption Although when first seen the rash has usually reached the vesicular stage if observed at the earliest stage of its development the chickenpox lesion appears as a small maculo papule This rapidly enlarges and becomes a vesicle *In the course of twelve to twenty four hours the* contents at first clear become turbid and pustular and at the latter stage some degree of umbilication may be observed The pustule then dries up to form a scab and after a varying period, from a few days to a week or two the scab falls off leaving a superficial pink or brown scar if the lesion has been well developed Later this becomes pearly white and in a fair proportion of cases permanent evidence of the attack is left Since the envelope of the vesicle is fragile it is frequently ruptured by the pressure of clothing and a firm brown scab is formed over the raw surface the lesion never arriving at the pustular stage Typically the vesicle or pustule is super ficially set in the skin oval in shape and irregular in outline its long axis running at right angles to the main axis of the body After its first appearance further crops of lesions continue to come out at irregular intervals for the next few days so that on any given patient all stages of the eruption are fre quently seen Usually appearing first on the trunk the face and scalp are also invaded and the rash is seen in its greatest profusion in these situations It appears also on the limbs but the density diminishes towards the distal parts so that in the average case lesions are relatively few or abortive below the elbow or knee Very occasionally cases are encountered in which the eruption comes out on the palms of the hands and the soles of the feet in the latter situation forming brown



Fig 5 Chickenpox erupt on on soles of feet

[*T fac p* 204



Fig. 51. Chickenpox eruption on fifth day to show distribution. Rash fully developed and in pustular stage



Fig 5 Chickenpox eruption on soles of feet

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discs not dissimilar to those seen in mild smallpox Unlike these however they are superficially set and disappear in the course of a day or two As might be expected the rash varies greatly in profusion and several cases have come under our notice in which the lesions were so profuse that the end of a lead pencil could hardly be set on the skin of the body without impinging on several In such cases however the grading in density can usually be made out from the centre of the trunk to the distal parts of the limbs or at the most profuse the density is no greater on the face forearms or wrists than on the trunk Lesions are often well seen on the palate faucial arches tonsils and buccal mucosa as yellowish sloughs and in these situations may be noted a few hours before they appear on the skin Though not influenced to the same extent as smallpox in its distribution by trauma or irritation nevertheless chickenpox may occasionally be affected by these factors and from time to time we have observed a special clustering of chickenpox lesions round the site of Schick reactions on the flexor surface of the forearm and on the thigh of a patient who had recently received an intramuscular injection of diphtheria antitoxin in that region

Constitutional disturbances are not extreme Many cases show no pyrexia but if the rash is dense there may be some irregular pyrexia in the eruptive period with a tendency to spiking during pustulation The patient complains of headache and malaise and suffers discomfort from the irritation of the pocks especially when the eruption is profuse in the mouth *Complications* are rare and mainly due to minor skin sepsis Apart from these *conjunctivitis* or *blepharitis* may occasionally be met with and though *nephritis laryngitis* and *broncho pneumonia* have been described they must be exceptional We have seen one fatal case in which *cavernous sinus thrombosis* followed directly upon sepsis of a chickenpox lesion of the forehead A fatal *streptococcal cellulitis* supervening upon the infection of a lesion with that organism has also been among our unusual experiences Of recent years a number of cases of *encephalo myelitis* following chickenpox have been reported and these conform generally in their manifestations to the condition which has been mentioned as a possible sequel to almost any of the acute infections *Relapse* is unknown and

second attacks though vouched for by competent observers must be exceedingly rare

Association with other Diseases Chickenpox may be found to run concurrently with any of the other acute infections but the frequency with which it is associated with *scarlet fever* cannot fail to attract the attention of those with much experience of fevers Ronaldson and Kelleher (1938) believe that this concurrence is not so common as statistics would suggest and are of the opinion that a faucial angina and peeling of the tongue are not differential whilst the supposition that subsequent desquamation will make a retrospective diagnosis is erroneous In certain cases no doubt what has been mistaken for scarlet fever has been in reality a scarlatiniform prodromal rash but on the other hand the diagnosis of concurrent chickenpox and scarlet fever often can be made quite confidently and it has been suggested that in some of these instances at least the scarlet fever is of the surgical type the chickenpox lesion having been infected by streptococcus pyogenes

A great deal of interest has been shown also in the relationship between *herpes zoster* and chickenpox since Bokay s (1909) observations stimulated enquiry Following these many instances of presumptive connection between these conditions have been reported and Ker (1920) grouped the cases according to their epidemiological relationship into those (1) in which herpes zoster is followed by chickenpox (2) in which chickenpox is followed by herpes (3) in which chickenpox and herpes is concurrent in the same individual and (4) in which chickenpox and herpes appear at the same time in different individuals presumably from a common source of infection The first group is by far the commonest according to Rolleston J D and Millar (1926) the third group being next common whilst the second and fourth groups are rare Rolleston believes that these various degrees of association are explicable on the basis of coincidence while Ker though willing to accept the last three groups on this basis considers that the evidence presented by the first group cannot lightly be put aside Le Feuvre (1918) believes strongly in the identity of the two conditions and he is supported by a number of others Although numerous cases of zoster have occurred in our own experience which have not been followed

by chickenpox nevertheless several separate ward outbreaks of chickenpox after herpes zoster have suggested that there is some common etiological factor Further help in elucidating the relationship was to be expected from the recent advances in the microbiology of the pock diseases and Brain (1933) has performed complement fixation reactions which bring evidence in support of the view that these two conditions are closely related and possibly identical Ronaldson and Kelleher (1938) however suggest that since an infective condition which reproduces chickenpox in contacts is a form of chickenpox the form of zoster giving rise to chickenpox should be termed varicella herpetiformis though they admit the difficulty in clinical differentiation

Varieties of the Disease Chickenpox is usually a benign infection but severe types may be encountered These however are very rare probably the commonest being the *gangrenous* form This occurs in weakly and badly nourished children in which the disease runs an apparently normal course until the scabbing stage is reached Instead of the scab falling off it becomes enlarged the surrounding skin is dusky and glazed and when the scab is removed an ulcer with thin undermined edges is revealed The necrosis continues with much destruction of underlying tissue and death is not infrequent In our own experience we have seen several ca es one fatal from which virulent C diphtheriae were isolated and it is possible that some at least of the cases classified as varicella gangrenosa in the past were the result of this secondary infection Banks and McCartney (1937) have reported a fulminating ca e in which the secondary invader was streptococcus pyogenes A *bullous type* is also described in which a number of the lesions are large in size and the constitutional disturbances severe Lastly a *hæmorrhagic* type occurs in which there is bleeding into the base of the pocks with purpuric lesions in the skin and bleeding from mucous surfaces The only case of this type which we have seen made a *complete* recovery but a fatal termination has been reported in instances in which the purpuric manifestations were widespread in the skin and mucous membranes

Diagnosis When chickenpox is epidemic there is little difficulty in making a diagnosis and even in sporadic cases the

second attacks though vouched for by competent observers must be exceedingly rare

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have seen Ronaldson and Kelleher (1938) are doubtful if the occurrence of desquamation in such cases necessarily means that a retrospective diagnosis of scarlet fever can be made Occasionally the presence of greyish yellow sloughs on the tonsils faucial pillars or palate before the eruption has appeared in the skin may cause the practitioner to suspect *diphtheria* In hospital practice the commonest conditions mistaken for chickenpox are various forms of *dermatitis impetigo herpes* and *pemphigus* Occasionally also the lesions of *urticaria papulosa* with oval-shaped papules crowned by a crust are confused with those of chickenpox

Prognosis Except when such clinical rarities as the gangrenous hæmorrhagic or bullous forms of the disease appear the prognosis must be regarded as uniformly favourable

Prophylaxis A quarantine period of 21 days is imposed on susceptible contacts In areas in which smallpox is epidemic chickenpox may be made notifiable for limited periods in order that visitation may be made for purposes of ensuring accuracy in diagnosis Active immunisation by the injection of chickenpox vesicle fluid has been attempted by several and one experiment has been favourably reported on by Biggar (1937) but in view of the possible risks following the injection of material which may contain pyogenic organisms the procedure can hardly be recommended Passive immunisation has also been the subject of investigation by various workers including Gordon and Meader (1929) and Gunn (1930) Whilst some degree of success has been claimed the results are inconstant and on the basis of our own experience with the method we would not place it in the same category as the corresponding procedure in measles This is unfortunate from the standpoint of hospital economics since chickenpox quarantines lead to considerable wastage of beds as may be realised from the fact in the two yearly period 1933–34 about 1 0 per cent of the North Western Hospital accommodation as expressed in bed days was continuously out of action from this cause or a loss of 1 460 bed days per annum

Treatment Very little in the way of treatment is necessary The patient is kept in bed for a few days until the temperature is normal Daily warm baths containing potassium permanganate and the dabbing of the lesions with a 1 per cent

distribution and morphology of the lesion do not leave much doubt as to its nature In exceptional cases the rash may be very scanty and cases have been described in which the lesions did not exceed one or two in number, but these must be very rare and the diagnosis provisional until the occurrence of obvious cases among the contacts supplies confirmation In our experience we have observed cases in which the rash consisted of one or two typical vesicles for about forty-eight hours after which however an eruption of average density appeared Very profuse rashes covering the extremities as well as the trunk and face may also be encountered occasionally but a careful consideration of the relative densities on the limbs as compared with the face and body will usually enable a diagnosis to be made

In *differential diagnosis* the most important distinction that requires to be made is from smallpox Owing to certain resemblances to smallpox of the mild epidemic type and to abortive attacks of the major type the differentiation of these from chickenpox may be a matter of some difficulty and great moment to the community In making a distinction chief emphasis should be placed on the distribution of the eruption and its order of development and for a detailed account of these the section on smallpox should be consulted The severity of onset, the density of the rash the age of the patient and features of the morphology of the eruption such as umbilication are in themselves unsatisfactory points on which to base a diagnosis In the prodromal stage of chickenpox it is frequently difficult to distinguish between a scarlatiniform rash and scarlet fever especially in the present mild type of the latter in which the rash may be the only characteristic feature Even when the chickenpox eruption is fully developed the presence of a scarlatiniform rash does not necessarily mean that it is prodromal for the diseases may co-exist The Schultz Charlton reaction may be of some assistance in such cases, and the finding of a profuse growth of streptococcus pyogenes in a throat swab or from pustular fluid would supply presumptive evidence that scarlet fever was present We must confess however that further observation of the patient in respect of tongue changes desquamation or the appearance of typical complications is frequently required although as we

CHAPTEP X

SMALLPOX

Synonym—Variola

Nomenclature Any modern account of smallpox must take into consideration the question of nomenclature to which a great deal of attention has been paid in England since 1931 The mild epidemic type which showed itself about that time caused doubts to arise as to whether the rigorous and expensive measures agreed upon by all as necessary to deal with the severe outbreaks of the past were really necessary for this benign infection and official recognition was given by the Ministry of Health to the fact that there are two epidemic types of smallpox types which experience has shown breed true and which do not change one into the other It is therefore now permissible to define the severe or classical epidemic type also described as the African as *variola major* and the mild or sub toxic variety also referred to as the American type amaas or alastrim as *variola minor* This terminology having been accepted by the 1929 Conference on the Nomenclature of Causes of Death and also by the Committee of the International Health Office in Paris it is now in order to employ these terms in official returns such as death certificates and to take cognizance of them in the practical methods applied to the control or eradication of the diseases At the same time the important fact should never be lost sight of that the disease remains the same clinical and pathological entity viz smallpox

Pathology It has been assumed that smallpox is caused by a virus and according to Ledingham (1934) it has now been satisfactorily demonstrated that the elementary bodies first observed by Buist in 1887 and again described by Paschen in 1906 and found in material from early vesicles and pustules constitute the actual virus When variolous or vaccinial material is inoculated into the rabbit s cornea a characteristic keratitis associated with the presence of Guarnieri bodies is produced These are now regarded as inclusion bodies resulting from the aggregation of Paschen bodies and rabbit cornea

dilution of the same substance help considerably in subduing pustulation and allaying the irritation of the rash Stubborn scabs may be removed with the starch poultice and the raw surface smeared with zinc ointment If lesions are profuse in the mouth a careful oral toilet should be performed and frequent mouth washes prescribed

and 1867 the age incidence has been chiefly in adults Of recent years and following the 1898 and 1907 Acts permitting conscientious objection infant vaccination has greatly fallen off with the result that as A F Cameron (1930) has suggested the disease has shown a tendency to revert to the younger age periods As a factor in mortality smallpox has varied widely Since 1856 the highest mean death rate per million from smallpox in England and Wales was during the quinquennium 1871–75 when it was 392 From that time till the end of the nineteenth century it declined steadily and except for a rise in 1901–05 when it was twenty five it has now become negligible as a cause of death this in spite of a widespread prevalence from 1921–32 As already noted however the disease during this period was of a mild epidemic type which in the words of Greenwood (1934) was characterized by a dissociation of fatality from superficial clinical signs That the appearance of this mild epidemic type was not a new phenomenon can hardly be doubted but the almost complete displacement of the classical and fatal type by a variant so mild and distinct in its manifestations (B M A Report on Immunization etc 1935) has had profound effects on the administrative attitude to the disease

The above general considerations having been dealt with it will be convenient to describe the main features of the two epidemic types separately bearing in mind that in each case we are dealing with the same clinical entity It is also to be borne in mind that in each case unless where stated to the contrary we are considering the natural disease that is as it occurs in those unprotected by vaccination

Variola Major

Transmission The source of infection is always a case of the disease but as in other diseases ambulatory or modified forms may occur so that the origin of infection is not always obvious Direct contact and droplet infection are responsible for infection in the majority of cases but infection carried by an intermediary or by fomites is also common A good deal of discussion has also taken place as to whether smallpox may be airborne for any considerable distance *e g* from a hospital to dwellings in the neighbourhood but the consensus of opinion is

scarification has been worked up into a diagnostic test for smallpox associated with the name of Paul (1919) In recent years much attention has been paid to serological reactions of the variola virus Thus Gordon (1925) demonstrated that the serum of a rabbit immunised against vaccinia virus gave specific complement fixation and agglutination reactions with this virus and also with that obtained from the lesions of mild or confluent smallpox but not with the virus of varicella These serological reactions have also been studied by Tulloch and his co workers (1929 and 1931) who have confirmed the fact that serologically bovine vaccinia vaccine lymph human vaccinia, variola major variola minor and generalised vaccinia of the rabbit *constitute a single entity They have also worked* out the details of a specific flocculation or precipitation test occurring when extracts of crusts from dermal lesions of variola major and minor are allowed to interact with anti vaccinia serum prepared in the rabbit This reaction seems *highly* specific the test distinguishing sharply between material derived from smallpox and vaccinial lesions on one hand and material from chickenpox on the other

The naked eye changes found at *post mortem* apart from the characteristic appearance of the rash at the stage at which death occurred are those of such complications as broncho pneumonia and toxic degenerative changes in heart muscle liver kidneys and spleen Localised inflammatory nodules with central necrosis are also found in the testes and are stated by Councilman and others to be characteristic of smallpox In hæmorrhagic smallpox hæmorrhages are found in the skin mucous and serous membranes and in muscular and connective tissues Hepatic enlargement with marked fatty degeneration is constant The heart muscle also shows well marked fatty change while the kidneys are pale and enlarged

Etiology Smallpox has a world wide distribution, and whilst the general epidemiological features have been modified in comparatively recent times by active immunisation in unvaccinated communities the seasonal incidence is chiefly *in the winter and spring* and children under five years show the highest age incidence In countries where infant vaccination is widely practised adolescents and adults are mainly affected and in England since the Vaccination Acts of 1853

outbreaks They are usually classified as erythematous hæmorrhagic or mixed in type The *erythematous* types frequently transient may be general or localised in distribution and scarlatiniform morbilliform erysipelatoid or urticarial in character When localised they show a preference for the region of the groins and armpits and even when general they tend to be accentuated in these areas Whilst the erythematous rash may not herald an attack of any particular severity when it is widely generalised and intense in character a severe and possibly toxic attack is to be apprehended Erysipelatoid rashes are of this character two fatal cases of the hæmorrhagic type seen in the Edinburgh outbreak of 1942 exhibiting this form of rash In another instance involving the face body and limbs was an intense dusky erythema giving a good imitation of a scarlet fever rash although the individual puncta were larger This also was the prelude to a hæmorrhagic attack Of the *hæmorrhagic* eruptions the petechial are the commonest and are said to be pathognomic of smallpox They consist of small hæmorrhagic punctations of varying degrees of profusion in the groins often described inaccurately according to Wanklyn as the bathing drawers rash and may be carried up on the flanks into the axillæ and on to the back Purpuric rashes are much less common and are usually associated with the hæmorrhagic type of the disease In *mixed* rashes petechial elements are found in much the same situation as above but the erythematous areas have a wider distribution Again certain forms of mixed rash proclaim a toxic type of smallpox In these the erythema is intense and generalised whilst scattered irregularly over the body are deep violet hæmorrhagic spots varying in size up to several millimetres in diameter

The initial stage usually lasts for three or four days but may be as short as two or as long as six whereupon the true or focal rash appears

Stage of Eruption The focal rash appears in the form of *macules* usually on the face the brow being first affected but this is not invariable as we have noted the first evidence of macules in the neighbourhood of the naso labial fold and the chin Again we have seen the first macules appearing on the sides and at the root of the neck In a few hours these become

now against this and the modern tendency is to attribute the occurrence of infection in such circumstances to defects in hospital administration It should be understood however that within the confines of a ward or room the virus may be airborne It is practically always inhaled but smallpox may also be transmitted by direct inoculation a few accidental cases of this nature usually being encountered when any wide spread epidemic occurs In the past also this method of infection formed the basis of the practice of *variolation* as a means of active immunisation

Infectivity Variola major is extremely infectious in this respect outrivalling all the other common fevers and while infectivity is probably greatest during the vesicular and pustular stages, it would probably be well to regard a case as capable of transmitting infection from the first symptom until the last crust has fallen off It is true that Ricketts and Byles (1908) were of the opinion that the pre eruptive toxæmic phase of smallpox was seldom infectious and gave it as their view that control measures were unnecessary for the contacts of cases whose illness terminated without an eruption but this has not been accepted by Gins (1924) or Cumpston and McCallum (1925) the latter being of the opinion that among their Australian cases the initial period of toxæmia had been infective A period of from six to eight weeks in hospital is usually required before the patient is free from scabs but in severe cases treatment may be prolonged for several months

Incubation and Quarantine Period The incubation period is very constant from 10 to 14 days a very common time being 12 days In the inoculated disease it is somewhat shorter from 8 to 10 days A quarantine period of 16 days is imposed on contacts of variola major

Clinical Features Stage of Invasion or Toxæmia The onset is abrupt with headache shivering or rigors nausea or vomiting backache and malaise The patient usually takes to bed and is feverish with dirty tongue foul breath and constipation At the onset with the temperature rising steeply to 102 or 104° F and with it an acceleration of the pulse and respiration the *primary or toxæmic fever* is initiated During this stage *prodromal or toxæmic rashes* are estimated to occur in about 10 per cent of cases though this appears to vary in different



Fig. 24. D[illegible]tribution [illegible] smallpox [illegible] on face [illegible] of body of [illegible] [illegible] [illegible] discrete in type [illegible] stage



Fig. [illegible] Distribution of confluent smallpox rash on face and upper extremities. Note [illegible] absence of lesions on lower [illegible]hest. The patient was in the thirteenth day of disease and [illegible] had taken place on the face while the rash was still in the pustular stage on the arms. A successful [illegible] [illegible] [illegible] also [illegible]

papules firm and shotty to the touch do not disappear on stretching the skin and are discretely set The full development of the rash from its first appearance is occasionally tardy and though it usually reaches this stage by the third or fourth day in some cases it will not be completely developed numerically till the fifth day When well out the focal rash is *generalised the distribution following certain well defined laws* It is most profuse on the face hands wrists and arms and back next on the chest and least on the abdomen On the feet and legs the eruption may be as thickly set as on the upper extremity although it may appear a little later than in the latter In distribution the great majority of cases will be

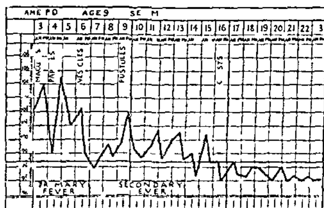


Fig 53 Temperature chart of case of unmodified variola major Note remission of temperature after primary fever

in conformity with this law the elucidation of which we owe to Ricketts but it is well to remember that anomalies are by no means rare and occasionally the density of the rash is influenced in various areas by anatomical prominences such as along the tendon sheaths on the back of the wrists by the pressure of a garment exposure to free movement or to some irritant such as a mustard plaster Conversely protected regions such as the axillæ are seldom invaded *The eruption* also invades the mucous membranes of the mouth pharynx and upper respiratory tract and even in the papular stage the presence of lesions in the larynx may give rise to the signs of laryngitis The *vesicular* stage develops in from thirty six to

forty eight hours after the appearance of the papules The vesicles are firmly set in the skin more or less circular in shape resistant to the touch and surrounded by a mild areola Although filled with clear fluid even at the earliest stage they *are greyish in colour in contrast with the waterpock appearance* of the corresponding stage in chickenpox They are small in size do not readily collapse on pricking and may show a central depression or umbilication During the development of the vesicular stage there is a greater or less remission in temperature which marks the end of the *primary or toxaemic fever*

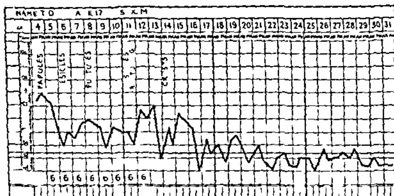


Fig 57 Temperature chart of severe confluent case of unmodified variola major Note remittent temperature curve of secondary fever The figures at the bottom are the doses in grams daily of sulphadiazin

In severe unmodified cases this fall though definite will not reach the normal whilst in mild cases with discrete rashes the patient *may remain apyrexial for one or two days* during which he feels comparatively well Throughout the three or four days of the vesicular stage the lesions increase in size the contents become turbid and finally altogether purulent so that the *pustular* stage is reached During this the pocks attain their maximum size, are hemispherical or conical in section the septa in the interior break down and if broken the contents ooze out When the rash is well marked a rise in temperature accompanies the pustular stage the *secondary or septic fever* of smallpox Certain patients with a scanty rash may show no definite pyrexial reaction characteristic of this

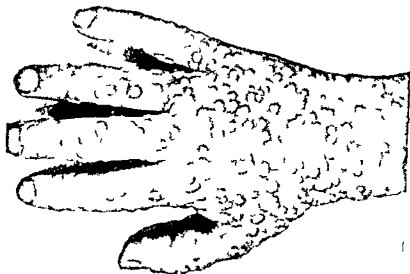


FIG. 56 Smallpox rash on ninth day of disease. Note circular shape of the lesions some of which show umbilication and oedema of hand

[*To face p.* 17

is obvious for weeks and scarring is quite definite pitting on the tip of the nose and the cheeks often producing an unfortunate appearance Unless there has been much wasting in the secondary fever the patient s strength returns rapidly but interruptions to convalescence may occur from boils otorrhœa adenitis and other localised pyogenic infections In seve e cases bedsores are not infrequent and considering the amount of skin destruction this is almost inevitable even with the most devoted nursing

Complications and Association with other Diseases In general smallpox is not a disease attended by frequent com plications and by far the most frequent are *boils* and *abscesses* which may occur in any part of the body and on one occasion we have encountered a *prostatic abscess* *Laryngitis* may be so severe as to require operation whilst chest complications such as *bronchitis* and *broncho pneumonia* may occur in severe cases Eye complications may be troublesome The conjunctiva and cornea are usually spared but infection may spread from lesions in the eyelids and set up purulent *conjunctivitis* and *ulceration* followed by opacities There is some disagreement among the authorities with regard to nervous complications Ker was of the opinion that these were rare whereas McCombie (1905) stated that in variola the nervous system is more often affected than in any other exanthem Peripheral neuritis and various forms of paralysis have been described whilst in recent years cases of *disseminated encephalo myelitis* have been reported In convalescence *erysipelas* may occur as an inter current infection

Relapse and Second Attack Relapse in smallpox is unknown and second attacks though extremely rare are well authent cated and are usually mild in nature

Varieties of the Disease To mild clinical types the terms *varioloid* or *modified smallpox* are usually applied These are commonly the result of residual immunity remaining from previous vaccination but though abortive or mild in character it should be remembered that they are capable of transmitting the disease in its most virulent form In mild cases the pro dromal stage may be well marked but the eruption is scanty and maturation though otherwise normal is speeded up or may advance no further than the vesicular or even the papular

phase and when present it shows all *gradations in extent from* a minor elevation of one degree lasting for a few days to a prolonged remittent temperature curve occasionally reaching 103° F and prolonged for two or three weeks With it is associated the constitutional disturbances appropriate to a septic condition irritability restlessness and sleeplessness During the early part of the secondary fever patients suffer considerable pain from the pustules and swelling of the face extremities and genitalia produce discomfort and stiffness The mouth and tongue are often dirty and swollen almost invariably there is a well marked catarrh of the upper respiratory tract which results in laryngitis a bronchitis with an irritable cough and pain on swallowing With the rupture of the pustules areas of the skin particularly of the face are covered with a foul smelling pus and the condition of the patient is one of great misery On the appearance of crusting however the general condition improves greatly the secondary fever begins to abate, and although the temperature may be kept up by local sepsis and boils convalescence is quickly established According to the profusion on the face the terms *confluent semi-confluent* and *discrete* are applied to the eruption *the severity of the illness being usually in direct proportion to* the density of lesions in this situation

Stage of Convalescence This lasts until all the scabs have been cast off Many separate rapidly and in patients with well marked eruptions it is no uncommon experience to find them lying in a pool of crusts In certain situations, *e g* the scalp they are so deeply embedded that they take weeks to come away even after the most assiduous attention with a scalpel On the soles of the feet and palms of the hands the hard skin offers obstruction to the escape of the pustular contents and these dry up to form brown discs or seeds which take a long time to reach the surface unless picked out The appearance in many cases of sub ungual discs which grow *out in the nail bed late in convalescence should not be over* looked as they often appear when convalescence has been nearly completed Quantities of hair may be shed in convalescence but even when there is considerable scarring in the scalp the amount of restoration may be surprising Pigmentation at the sites of the lesions, even when these are scanty

stage secondary fever being absent. Again the eruption may be profuse and the initial fever of some severity when suddenly at the papular stage modification of the usual process of maturation occurs resulting in morphological changes in the character of the lesions themselves. They become prominent, conical and fleshy with on their summit a short lived vesicular stage merging into rapidly crusting small yellow pustules. Again the individual lesions of scanty eruptions may conform to the usual description with a well marked areola but remain superficial or show irregularity in size and shape. Occasionally the disease may terminate at the end of the stage of invasion without the appearance of an eruption but it is difficult to understand how the clinical diagnosis of such cases could be fully substantiated.

The terms *hæmorrhagic toxic* or *malignant smallpox* are applied to the severest forms of the disease which must be assumed to be the result of infection of an individual with a complete lack of immunity by a virus of high pathogenicity. Even in limited outbreaks they may form a high proportion of the total and in the Edinburgh epidemic of 1942 no fewer than 6 out of 36 cases were of this type. The initial stage is very severe profound prostration being accompanied by rashes of the petechial or intense generalised erysipelatoid or scarlatiniform type. Soon deep violet hæmorrhages 3 to 5 mm in diameter appear irregularly over the body while larger purpuric blotches may also be seen. Copious bleedings of the nose mouth bowel or uterus may occur and in some cases the patient cries out with the intensity of lumbar pain. Blebbing of the skin containing blood stained serum may precede death which occurs before the focal rash has time to appear. From these blebs Wilkinson (1943) has made the interesting observation that in his cases of this type of the disease hæmolytic streptococci could always be grown in pure culture. In certain patients hæmorrhage is delayed until the eruptive stage. These are seen to be critically ill from the beginning with a dusky confluent rash. In the later papular or early vesicular stage hæmorrhages occur into and around the lesions while large petechiæ ranging from indigo violet to bright red may be profuse over the skin unaffected by the rash. Consciousness may be retained almost till the end which again

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The terms *hæmorrhagic toxic* or *malignant small* applied to the severest forms of the disease, which n *assumed to be the result of infection of an individual* complete lack of immunity by a virus of high pathoge Even in limited outbreaks they may form a high propor the total and in the Edinburgh epidemic of 1942 no fewe 6 out of 36 cases were of this type The initial stage i severe profound prostration being accompanied by ras the petechial or intense generalised erysipelatoid or tiniform type Soon deep violet hæmorrhages 3 to 5 n diameter appear irregularly over the body while larger pu blotches may also be seen Copious bleedings of the mouth bowel or uterus may occur and in some case patient cries out with the intensity of lumbar pain Bl of the skin containing blood stained serum may precede c which occurs before the focal rash has time to appear these blebs Wilkinson (1943) has made the interesting ob tion that in his cases of this type of the disease hæmo streptococci could always be grown in pure culture certain patients hæmorrhage is delayed until the eru stage These are seen to be critically ill from the begi with a dusky confluent rash In the later papular or vesicular stage hæmorrhages occur into and around the le while large petechiæ ranging from indigo violet to bright may be profuse over the skin unaffected by the rash c sciousness may be retained almost till the end which

may be preceded by hæmorrhages from mucous surfaces and the assumption by the skin of a smoky appearance Or again the skin hæmorrhages may be confined to the vesicles which have taken the usual time to develop but here again intractable hæmorrhages from the nose or rectum precede death although Goodall reports recovery as occasionally occurring in this type In hæmorrhagic smallpox death is usually ascribed to heart failure but according to Ricketts although the pulse is poor and the myocardium gravely affected death results from pulmonary œdema

Also into the category of severe types must be brought the *confluent case* which though it does not differ in any respect from the average case already described except in the profusion of the eruption this in itself gives the confluent case a character of its own and produces an illness of great danger The confluence of the rash may be suspected even in the papular stage more by palpation than inspection of the skin of the face but this feature may not be evident until the rash has been in the fully developed pustular stage for one or two days viz on the eighth or ninth days of eruption although patches of confluence may appear round the nose a day or two earlier At this point the appearance of the patient is dreadful the face covered with a continuous layer of pustules greatly swollen with lips protuberant and sharing in the pustulation The faucial buccal and palatal mucosa is inflamed and covered with sloughs and the tongue swollen dirty and fissured The patient complains of pain on swallowing some degree of laryngitis results in hoarseness and he may be worried by a harsh painful cough The appearance of the face is repeated on the upper part of the back the extremities and to some extent on the chest and genitalia The patients general condition is miserable in the extreme the secondary fever being as well marked as the primary in all confluent cases is at its height and the temperature may reach levels of between 102° and 105 F The pulse is rapid and compressible and respirations are accelerated Though in a low moaning semi stupor the patient can be roused and may even take nourishment amazingly well With the advent of crusting on the face the pain of the eruption on the face and hands becomes more bearable but by this time an intense inflammatory reaction



Fig. 58 Appearance of face on twelfth day of confluent smallpox

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Consequently in 1840 the practice was abolished by law in the United Kingdom

Variola Minor

Transmission Whilst in our own experience this epidemic type has been spread by an intermediary or fomites the mode of transmission is usually by close and continuous contact and according to McSweeney (1931) casual contacts are unlikely to be infected

Infectivity This is much less than that of variola major and in individual cases A F Cameron (1932) has suggested that it is proportional to the profusion of the eruption The patient is potentially infective from the first symptom and remains so till the last crust has separated on the average this taking three to four weeks

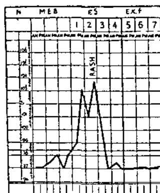


FIG 53 Temperature chart in case of variola minor in unvaccinated patient Secondary fever absent

Incubation Period and Quarantine The incubation period usually falls within ten to fifteen days but periods of eighteen and twenty one days have been recorded and consequently quarantine or supervision of contacts is maintained for three weeks

Clinical Features In his series Marden (1936) *reports that only 8 51 per cent of patients* gave no history of symptoms prior to the outcrop of the focal rash the great preponderance showing a definite initial illness The onset is sudden with well marked elevation of temperature to 101 or 104 F headache backache vomiting chills pains in limbs sore throat and nausea being the commonest features The febrile disturbance continues for two to five days but usually by the third or fourth day the temperature becomes normal and the patient may feel well Hæmorrhagic and erythematous prodromal rashes are occasionally seen

Stage of Eruption McSweeney (1931) is of the opinion that the rash never appears before the third day but Marsden (1936) found

appears on the normal skin in areas where the rash is less dense and this together with bleb formations resulting from the coalition of groups of lesions on the arms or back results in extensive exfoliation of the cuticle which is thrown off in sheets leaving a dirty granulating surface During this stage wasting is rapid As scabbing proceeds over the body the general condition improves and this is reflected in the expression of the eyes which clear and alert in the spectacle shaped normal skin of the orbits seems somewhat incongruous in the *almost continuous scab encasing the rest of the features* Pocks on the distal parts of the extremities do not always undergo the process of rupture and scabbing in a number the contents seem to diminish the pock becomes flabby and eventually dries up to form a seed in the substance of the skin rather than an excrescence in the shape of a crust This process is most noticeable on the lower legs and dorsum of foot With the casting off of scabs the general condition rapidly *improves sleep appetite and weight are regained* and in spite of extensive skin destruction healing is remarkably rapid In the confluent case boils and abscesses are particularly liable to occur and scarring is extensive particularly on the nose cheeks and chin Death in these cases occurs about the tenth or twelfth day from myocarditis and circulatory enfeeblement the latter resulting before death in failure to react with secondary fever and in the comparative failure of lesions to develop on the distal part of the limbs

Variolation This method of producing active immunisation although practised by many primitive communities from earliest times is now only of historic interest It was performed by applying to a scratch in the skin material from a smallpox vesicle preferably from another variolated case If successful on the fourth day a cluster of vesicles appeared at the site of inoculation subsequently becoming pustular about the eighth day At this time the symptoms of the invasion period of smallpox appeared and about the eleventh day a generalized smallpox eruption appeared and ran its usual course The inoculated disease was usually in the modified or discrete form but sometimes a severe or fatal attack resulted Moreover the inoculated disease was infectious so that epidemics of smallpox might be started

Marsden s statement it would clearly be injudicious to place too much reliance on this point in distinguishing between the two epidemic types Death is an infrequent termination to variola minor fatal cases usually occurring in those already suffering from other serious illness

Complications Various *pyococcal skin infections* arise in convalescence but A F Cameron (1932) states that *corneal ulceration* and opacities constituted the only important com plications *Post variolar encephalitis* was seen by Marsden in seven instances of which three proved fatal among the 13 686 cases of variola minor admitted to the London smallpox hospitals during the 1928–34 epidemic

Main Differences between Variola Major and Minor From the descriptions given above it will be seen that variola minor differs from variola major chiefly in the following character istics Its infectivity is much less and its incubation period may be prolonged The initial period is less severe the rash is usually less profuse and may be very scanty maturation is more rapid secondary fever is uncommon and not great in amount Mortality is negligible It is equally evident that a study of single cases does not enable a classification into one or other of the epidemic types to be made

Diagnosis Just as early diagnosis is all important for the individual attacked by diphtheria so is the early diagnosis of smallpox all important for the community in which it appears because early recognition is necessary for adminis trative action to be effective Ricketts (1900) has observed that smallpox is a disease in which a certain diagnosis can be arrived at in almost every case but he prefaces this by remarl ing that it presents more difficulties in its detection than most other diseases These Wanklyn (1913) ascribed to the fact that commonly the possibility of the presence of smallpox never enters into the mind of the medical attendant and while in these days of international arrangements for the rapid dis semination of information regarding the occurrence of infectious disease together with the careful surveillance exercised by port medical authorities we may believe there is much less chance than formerly of smallpox appearing suddenly and unex pectedly nevertheless it would be unwise to allow it to pass out of mind altogether In diagnosis all who have written

definite percentages in whom the eruption came out on the first and second day, although in a substantial majority the third and fourth days were the favourite days of appearance It may however, be delayed until the seventh or eighth day and Garrow (1924) has reported cases as late as the 10th day *The first lesions usually appear on the face a few hours later* they are seen on the forearms and trunk, and within twelve hours the legs are affected, the distribution conforming exactly with that of the major type Occasionally the first lesions have been reported on the chest and back The eruption does not come out in crops although some have suggested this the slightly more advanced stage of the lesions on the face as compared with those *on the legs being in conformity with the* evolution of all smallpox eruptions whether of the major or minor type It goes through the usual stages of evolution but maturation is more rapid The *papular stage* lasts for thirty six to forty eight hours Marsden (1936) describing the papule as unobtrusive pin head in size and sensible to touch *Vesiculation* appears on the third day vesicles being sometimes irregular in outline and although comparatively superficially set in the skin fairly firm to the touch and not hemispherical as in variola major This stage is usually short lived seldom more than twenty four hours and by the fourth day pustulation *has begun The rash attains its height by the fifth or sixth* day and by the seventh or eighth day scabbing will have commenced on the face but it may take longer to appear on the extremities Usually the scabs have fallen away by the end of the third or fourth week but in confluent and semi confluent cases they persist for six or eight weeks and sometimes even in mild cases seeds may remain in the soles of the feet for many weeks Scarring is not so deep as in variola major and Marsden (1936) notes that in over 11 per cent of patients on leaving hospital pigmented scarring was noted whilst in a few pitting on the face was evident Differences in their *findings in respect of the occurrence of secondary fever* in variola minor has been reported by various writers Thus McSweeney (1931) never observed it among Cardiff cases while Marsden (1936) found it in 5 32 per cent of London cases Whilst it is clearly *a feature absent from the course* of the disease in a very large proportion of patients in view of

given time the lesions are at the same stage of development and the fairly constant period taken to reach the various stages is of great importance and careful observation of these features will be most informative

In the *prodromal* stage and in the absence of a history of exposure diagnosis is impossible on the grounds of signs and symptoms alone the onset of an acute febrile disturbance being usually ascribed to *influenza* Should a prodromal petechial rash appear involving the flexures of the groins the diagnosis of smallpox becomes a practical certainty Scarlatini form prodromal rashes may suggest *scarlet fever* but throat and tongue signs would be absent in the initial stage of smallpox The presence of respiratory catarrh and Koplik spots would serve to distinguish between *measles* and a prodromal morbili form rash but confusion with measles is much less likely at this period than in the *papular* stage of the true eruption According to Wanklyn the skilled observer is more likely to be misled than the inexperienced in the last mentioned as the measles rash when full out on the face may bear an extra ordinary resemblance to smallpox In variola major the rash may show confluence even in the papular stage but a well marked rash of this type would be expected to present shottiness though this is not always a reliable guide in either the major or minor forms and variola major rashes confluent at the papular stage on occasions have been described as velvety to the touch The distribution however will settle the point as well as the presence or absence of Koplik spots On examination of the buccal and faucial mucosa the characteristic yellow sloughs of the vesicular stage of smallpox may be present at this stage of the eruption Also at this stage in smallpox the temperature will be coming down and the patient s condition ameliorated whereas in measles the febrile and constitutional disturbance is at its maximum In the papular stage various *syphilitic* rashes may require to be distinguished from both variola major and minor but in these apart from the Wassermann test the absence of pyrexia the presence of generalised adenitis and the distribution should make the diagnosis clear *Papular urticaria* may also be confused with minor smallpox but again careful observation of the distribution and maturation of the eruption will exclude

about the disease in modern times have accepted without question Ricketts emphasis on the distribution of the focal eruption and this remains the sheet anchor in diagnosis whether the epidemic type in the course of which the individual case occurs is major or minor smallpox In this connection however two points must never be lost sight of It has already been pointed out that the complete development of the true rash from its first appearance is tardy, and it will not be wholly out till the third fourth or even the fifth day It may not be possible therefore, to assess the full significance of the distribution until a few days have passed and moreover, if the patient is the first in an outbreak it is most unlikely that a diagnosis will be made until this stage has been reached It must be realised therefore that while practically all cases of smallpox can be so classified eventually, this will only be possible in a certain proportion after a sufficient period of observation has elapsed In determing the exact significance of the distribution few real errors would occur if Wanklyn s precept could always be borne in mind namely that lesions are present in ascending order of density on abdomen chest back arms and face This author also recommended that in cases which were not perfectly straightforward a diagram of the distribution should be made as he had found this a surprisingly useful aid to diagnosis The other point to appreciate in respect of distribution is that this feature of the rash may be so modified by previous vaccination that the total number of lesions may be very small In this connection it should scarcely require to be emphasised when so much depends on ascertaining the distribution of the rash that the whole of the skin surface should be thoroughly examined Although attributing first importance to distribution the morphology of the lesions and their mode of maturation as a whole should not be overlooked Such points as shape umbilication shottiness whether multi or unilocular are in themselves very insecure foundations on which to base a diagnosis but taken together these features will assist in the decision for or against smallpox since even in the most attenuated rash there may be one lesion which in its characteristic morphology and evolution will provide the clue to diagnosis The gradual evolution of the eruption monophasic in the sense that at any

population *vaccinia* lesions resulting from auto or hetero inoculation especially in those suffering from seborrhœa or eczema may give rise to difficulties in diagnosis In such circumstances the morphology of the eruption is exactly that of smallpox and when the vaccinal material has been implanted on raw weeping surfaces the result of old standing eczema the clinical picture produced is exactly that of confluent smallpox and in addition there may be considerable constitutional disturbance The distribution however will supply the answer to the problem Finally in the examination of any case suspected to be suffering from smallpox the *state of vaccination* may be of assistance in diagnosis The annual tables given in the Reports of the Chief Medical Officer of the Ministry of Health showing the distribution of smallpox cases according to age and vaccinal state point to the almost complete absence of smallpox in vaccinated children under ten and in persons under twenty who have been successfully re vaccinated The presence of vaccination and re vaccination scars at these age periods therefore practically excludes smallpox

Diagnosis by Vaccination From his observations on the results of vaccination performed at various stages in the incubation initial and eruptive periods of smallpox Ricketts concluded that successful vaccination done on the day of emergence of the true rash would not be conclusive but that successful vaccination performed three days after the appearance of a doubtful rash would exclude smallpox That this rule holds in variola minor is disputed by some but in Marsden s (1936) opinion successful vaccination during convalescence from variola minor should cast the gravest doubt on the accuracy of the original diagnosis Moreover with respect to vaccination after the outcrop of the focal rash he found no fundamental difference between the behaviour of variola minor as compared with that of variola major

Laboratory Diagnosis Although the diagnosis of smallpox may be established in the laboratory by the production of lesions in susceptible animals serological procedures and staining of films from suspected lesions it is with the two latter that the laboratory worker is now concerned Agglutination precipitation and complement

smallpox Cases of smallpox in the early papular stage with meningism may closely resemble cerebro spinal fever It may not be possible on one lumbar puncture to exclude the latter and the only course open may be to await further developments In the *vesicular* stage the disease most likely to be mistaken for smallpox is *chickenpox* and the differentiation of these two diseases is the most important point in diagnosis Below are tabulated the main contrasting features but it should be clearly recognised that the eruption of smallpox is not merely an inversion of that of chickenpox, *e g* there may be little or no lessening of the density of the smallpox rash on the upper extremity as we pass from the wrist towards the axilla whereas in chickenpox there is usually a gradual fading in density from the proximal to the distal parts of both extremities Also the density on the upper part of the back in smallpox may be as great as that on the arms Lastly, the presence of lesions on the palms and soles does not in itself make the diagnosis of smallpox

Smallpox	Chickenpox
1 Distribution centrifugal In both major and minor types density greatest on face next on arms and then on back Tends to spare flanks and axillæ and prominent on exposed parts First seen on brow face and wrists	1 Distribution centripetal Density greatest on trunk and face least on extremities and absent or scanty on forearms and legs Present on flanks and axillæ and no special preference for exposed parts First seen on trunk
2 Character Round and deeply set in major type In minor type or the modified major type may be irregular in shape but gives impression of being *in* the skin at vesicular stage No true cropping in either type but monophasic in development	2 Character Oval thin walled irregular in outline superficial in skin Definite evidence of cropping

Bromide and iodide eruptions may sometimes simulate the smallpox eruption but the differences in distribution and the slow maturation of the drug rashes should decide the diagnosis *Pustular syphilides acne* and *impetigo* may present certain resemblances to smallpox especially variola minor but whilst in these the distribution is not that of smallpox it should be remembered that the diseases may co-exist During epidemics when mass vaccination is being carried out in the general

population *vaccinia* lesions resulting from auto or hetero inoculation especially in those suffering from seborrhœa or eczema may give rise to difficulties in diagnosis In such circumstances the morphology of the eruption is exactly that of smallpox and when the vaccinal material has been implanted on raw weeping surfaces the result of old standing eczema the clinical picture produced is exactly that of confluent smallpox and in addition there may be considerable constitutional disturbance The distribution however will supply the answer to the problem Finally in the examination of any case suspected to be suffering from smallpox the *state of vaccination* may be of assistance in diagnosis The annual tables given in the Reports of the Chief Medical Officer of the Ministry of Health showing the distribution of smallpox cases according to age and vaccinial state point to the almost complete absence of smallpox in vaccinated children under ten and in persons under twenty who have been successfully re vaccinated The presence of vaccination and re vaccination scars at these age periods therefore practically excludes smallpox

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fixation reactions may be performed by observing the effects of *known antisera on antigens derived from lesions* According to Tulloch (1932) complement fixation is the most delicate but great precision is needed before uniform results are to be looked for Marsden (1936) however places considerable reliance on the flocculation test, which in his series of cases of variola minor gave results unapproached by other laboratory methods The complement fixation and flocculation tests however suffer from the drawback that vesicular fluid or scabs from the patient are required and at this stage in the disease the clinical diagnosis will probably have been made The disadvantage of this time lag is obvious but Van Rooyen and Illingworth (1944) have devised a method which can be applied on the first days of the rash Films are made from the scrapings of lesions and stained by a special method to show elementary bodies The distinction between variola and varicella is that the former are larger and can be readily demonstrated in the macular papular and vesicular stage of the disease Obviously if the claims made on behalf of this procedure are substantiated a very valuable advance in smallpox diagnosis will have been made

Prognosis This depends on the three main factors of epidemic type state of vaccination and age of the patient Epidemic type may be considered of first importance because irrespective of the other two factors the prognosis is practically always favourable in variola minor In the years 1922–29 *inclusive* in 60 888 cases of variola minor in England and Wales the death rate was 3 40 per 1 000 cases This may be compared with the death rate in England and Wales from variola major between 1911–20 inclusive when it was 94 83 per 1 000 or with that of 160 per 1 000 in London in 1902 It follows from the above that the other two factors of state of vaccination and age only require consideration in so far as they affect prognosis in variola major With regard to the former McCombie s often quoted figures show that in the M A B hospital cases whereas in vaccinated patients under twenty years of age the case fatality was 1 30 per cent in the unvaccinated it was 26 0 per cent , while for those over twenty it was 9 3 per cent in the vaccinated and 35 6 in the unvaccinated Turning to the effect of age on prognosis it is found

that the fatality rate of unmodified variola major in children under five is about 40 per cent falls during the next ten years age period thereafter increasing till after forty years it may be greater than in young children In individual cases very bright erysipelatoid or hæmorrhagic prodromal rashes usually point to a severe oncoming attack In the hæmorrhagic clinical type death is practically invariable between the fifth and tenth days The severity of other cases depends on the profusion of the eruption various writers being in agreement that confluent cases show a 60 or 70 per cent case fatality semi confluent under 10 per cent and discrete under 5 per cent Such fatality rates apply to unprotected individuals as in cases in which the rash is confluent previous vaccination even at some remote period may be expected to give a more favourable aspect to prognosis If death occurs from smallpox it usually does so from heart failure following exhaustion or pneumonia

With regard to prognosis in *pregnant* women all are agreed that the occurrence of the unmodified form of variola major is a serious event abortion being frequent in severe types and supervening in about one third of the more moderate attacks In variola minor abortion is much less common and Marsden (1936) regards this as rather surprising in view of the undoubted tendency to uterine hæmorrhage evinced by many women at the outset of their attacks of this form of the disease He believes however that the onset of smallpox did play some part in the induction of labour during the last two months of pregnancy in a number of his cases The effect on *infants* of the development of variola minor in mothers about the time of parturition has been studied by Marsden and Greenfield (1934) Their observations indicate that infection in utero is more or less of an accident but if it occurs the infection of mother and child is not simultaneous the child showing an incubation period corresponding to that of inoculation smallpox the time of infection corresponding to the immediate pre eruptive period Should the child escape then it might similarly acquire infection at or about the time of separation from its parent this being particularly liable to happen if the mother s rash was in its early stages when birth took place If the child escaped these two contingencies in the absence of

prompt successful vaccination infection acquired by the usual method of inhalation generally showed itself after the normal incubation period Finally a fœtus escaping congenital infection and remaining in utero until the mother is convalescent may be borne immune i e refractory to vaccination but Marsden and Greenfield are careful to point out that the immunity may have been the result of an intrauterine attack leaving no superficial evidence Many cases are on record in which children in like circumstances, have been born with typical smallpox scars

Prophylaxis The procedures applicable to the prevention of smallpox are notification isolation in special smallpox hospitals and terminal disinfection of premises clothing and bed clothes and every single article which has been in possible contact with the patient These measures supplemented by and as A F Cameron (1932) has pointed out really *dependent* on prompt vaccination and re vaccination of contacts have proved efficacious in limiting the spread of variola major During outbreaks careful attention should be paid to the immediate contacts since among these missed cases who still show evidence of the disease in the shape of scarring and pigmentation may have been responsible for the infection Immediate vaccination should be offered to all contacts and *careful quarantine and supervision imposed for sixteen days* in a reception house if possible on all familial and intimate contacts School closure is not required and the exclusion of contacts from school will obviously depend on their state of vaccination It has also been found very useful to make chickenpox notifiable since it is usually mistakes in diagnosis of the latter which are responsible for missed cases continuing *to spread infection* The last mentioned measure is of little value however unless a practitioner experienced in the diagnosis of smallpox and chicken pox examines the cases and verifies the diagnosis Isolation has always been carried out in this country in recent times in special hospitals set apart for smallpox these being far removed from thickly populated areas though in several of the large provincial centres it has been considered expedient to have the smallpox hospital though a separate unit for administrative purposes situated in close proximity to the fever hospital In smallpox

hospitals 2 000 cubic feet per patient has been laid down as a standard of accommodation careful precautions must always be taken in respect of vaccination and re vaccination of staff and special arrangements are necessary for the disinfection of the persons and clothing of all who leave the hospital All these measures while absolutely necessary in variola major impose a burden on the financial resources of local authorities and a strong body of opinion has grown up in England as a result of recent experience of the minor epidemic type of the disease that in outbreaks of this type less elaborate procedures are justifiable In a report on the subject (Reports on Public Health and Medical Subjects No 62 1931) the Ministry of Health has outlined certain modifications of the ordinary procedure which might be considered by local authorities when confronted by variola minor In this it is suggested that on the occurrence of the first cases in any given outbreak the usual strict measures should be applied The observation of a small number of cases will usually determine the epidemic type and should it prove to be variola minor local authorities need not continue to carry out all the procedures necessary for major smallpox A policy of strict isolation in hospital of all cases need not be adhered to and in this connection the observations of A F Cameron (1932) on the basis of his experience of the London epidemic of variola minor in 1929–32 are of the highest value He stated that not more than 14 per cent of all cases removed to hospital were in need for this form of treatment and is of the opinion that a process of selection should be applied the case with 100 lesions on the face to receive consideration and those with 300 or more usually to be selected other cases which could reasonably be isolated at home and where all occupants are protected by prompt vaccination should not be removed He also suggests that if necessary nursing assistance might be provided The Ministry Report also raises the question of the advisability of treating patients suffering from variola minor in an isolation block or in special wards of a fever hospital where the staff is fully protected by vaccination and the administration of the hospital in every respect careful and thorough Since there is frequently difficulty in diagnosis practitioners should be circulated with up to-date clinical accounts of variola minor and provision

made for the services of smallpox consultants Vaccine lymph should be made available to practitioners for the vaccination of suspected cases and contacts The supervision of contacts should be limited to those who have been in close relationship with the patient from the moment of his first symptom until the appearance of his rash or isolation, and personal visitation of contacts may be replaced by notices from the Medical Officer of Health Consideration of this modified procedure indicates how far the views of public health workers have changed since 1920 in relation to smallpox as a result of the epidemic of variola minor which appeared in England and Wales about that time This change has been pressed upon them by the logic of events but it is essential that there should be no confusion of thought as to the measures necessary for the prevention of variola major The possibility of the introduction of this type into a community should never be lost sight of either by itself or coincident with the minor type Moreover it would be well to bear in mind the Ministry's recommendation that there should be maintained the popular and unbiased education of the population of the safeguards which the individual can obtain by vaccination against any form of smallpox

Treatment Attempts at *specific* treatment have been made by the injection of bovine antivaccinial serum but the results are not striking while others have tried human convalescent serum with similar results Wilkinson (1943) however regards the administration of convalescent smallpox serum taken from the donor between the fourth and sixth weeks after onset of smallpox as promising and believes that it might conceivably be of benefit in the toxic phase of the illness In view of the sepsis which is such a prominent element in smallpox *chemotherapy* with the sulphonamide drugs has been employed among *others by the above named worker who is of the* opinion that sulphanilamide is of undoubted value in the treatment of septic complications We have had the opportunity of treating a small series of cases of variola major with sulphanilamide sulphapyridine and sulphathiazine and are in agreement with other observers that no effect on the hæmorrhagic form of the disease or on the toxæmic phase of other types was produced Some have claimed a significant reduction

in mortality rates in confluent smallpox but our number of cases of this type was too small to permit of the application of this critical test while there was no demonstrable effect on the evolution of lesions or on secondary fever There was however an almost complete absence of eye and lung com plications even in severe confluent cases and there was remarkably rapid healing of raw surfaces after exfoliation of cuticle when treated by the application of jelonet gauze and sulphonamide powder the destruction of the true skin being apparently limited It would appear logical therefore to initiate sulphonamide treatment at the vesicular stage with heavy doses 9–12 grms per day and continue on a diminishing scale for ten days with the usual precautions of giving abundant fluids and watching the urine carefully Apart from this treatment is largely symptomatic *Diet* during the primary fever should be fluid consisting of milk augmented by one or other of the patent foods With the remission of temperature following the primary fever the diet should be up to the limit of the patient s capacity and in certain cases even of the confluent type the appetite may remain remarkably good such patients in our experience being able to cope with what amounted practically to a full mixed diet throughout the whole of a severe and exhausting secondary fever *Discomfort in swallowing* may be alleviated with a cocaine spray to the throat immediately before meals whilst iced drinks and ice cream may be more readily tolerated in this phase From the commencement of the illness a routine of frequent conscientious attention to the *toilet of the eyes mouth and nose* should be established and throughout the illness *assiduous attention to the skin* is essential Innumerable preparations have been recommended for application to the skin lesions We prefer dusting with a powder containing iodoform and boric acid or painting with a watery solution of potassium permanganate but ointments containing carbolic acid or painting the lesion with tincture of iodine are favoured by some Frequent *warm baths* containing potassium permanganate or dettol should be given as soon as the patient is able to take them and if arrangements can be made the continuous warm bath is highly spoken of At the stage when the lesions are irritating or painful boric lint soaks

kept moist with iced water or an acriflavine emulsion in an oily basis are useful especially on the hands and face For *headache*, cold applications to the head should be made, and for restlessness and *insomnia* chloral and bromide, or barbiturates will be required Tepid or cold sponging will also help in these states especially when the temperature is high but in the more marked forms of *delirium* morphine or morphine and hyoscine compound are necessary and in *addition the patient must be strictly watched For backache* hot fomentations are the usual remedy *Laryngitis* is treated by the steam tent and hot fomentations to the neck and tracheotomy will have to be performed in certain cases In convalescence various forms of skin sepsis and inflammatory conditions of the eye may require treatment on the usual lines A problem may be presented by the appearance of sub ungual discs late in convalescence Some have expressed doubts as to their power of infecting others but it is well to take no risks and they should be dealt with by filing the nail down to the level of the disc whereupon it is easy to dispose of the fine dry powder of which it consists The removal of scabs in such situations as the scalp can be hastened by careful digging out with a scalpel but some of the small deeply embedded crusts left after abortive eruptions present difficulties *Something can be done to hasten their removal by means of* starch poultices, but time is the main factor in completing exfoliation In wards where severe smallpox is being treated *deodorants* are usually required even when the most thorough ventilation is possible

CHAPTER XI

VACCINATION

Vaccinia or Cowpox is an infectious disease occurring naturally in bovines and a brief recapitulation of its main features is necessary before proceeding to a consideration of human vaccination It causes vesiculation and ulceration of the udders and teats and a similar condition occurs in horses sheep goats swine and fowls but the exact relationship between the pock diseases of various animals is still obscure Cowpox is transmissible from animal to man and although relatively rare in the United Kingdom at the present time examples of naturally acquired infection are occasionally encountered in the shape of vesicles and pustules on the fingers and hands of cowmen and milkers These lesions are associated with lymphangitis and constitutional disturbance whilst in morphology and development they are essentially the same as those resulting from vaccination Owing to their rarity they may puzzle the practitioner

Relationship of Vaccinia to Smallpox It had been noted that persons who had suffered from cowpox escaped small pox and Jenner put this to the proof by first inoculating a human subject with cowpox A few months later he failed to induce variolation in the same person and in 1798 when he published his work the foundation of vaccination as a method of protection against smallpox was laid Early experimental work indicated that the virus of vaccinia and variola were identical S M Copeman (1902) produced variolation in monkeys by the inoculation of material from human cases of smallpox and found that inoculum from the monkeys when injected into cows after several passages finally produced lesions similar to those of cowpox Whilst the immunological work of Gordon (1925) and Craigie and Tulloch (1931) has further confirmed the relationship between the virus of small pox and vaccinia more recent work has tended to disclose differences by means of serological analysis Thus Amies (1932) demonstrated differences in the agglutination reactions of vaccinia on one hand and variola whether minor or major

on the other Again the work of Downie (1939) would indicate that bovine cowpox is not derived from humans infected with variola or vaccinia as had been thought but is a disease *sui generis* and even that natural cowpox is not identical with vaccinia All though containing antigens in common also possess antigens specific for the homologous virus whilst there are also histological differences between the experimental lesions produced by strains of cowpox and vaccinia virus

Nature of Vaccinia Virus Whilst these recent studies appear to cast doubt on the identity of variola, cowpox and its derivative vaccinia virus it is unlikely that their validity extends beyond the laboratory The original conception that vaccinia virus was a variant of variola virus resulting from animal passage still holds, and the fact remains that the most important feature of vaccinia virus is that it shares with variola virus the specific property of producing active immunity to smallpox Other important characteristics are that in vaccinia skin lesions remain localised to the site of inoculation, that it is non infective in the sense of smallpox, and is incapable of producing that disease It is now generally recognised that the elementary bodies first observed by Paschen (1906) in vesicle fluid from vaccinia are identical with the casual organism of the condition and various workers including *Rivers (1931) and Goodpasture and his co workers (1932)* succeeded in growing vaccinia virus on chicken embryo tyrode medium and the chorio allantoic membrane of hens eggs On these media it has been carried through numerous generations Reference is made below to its immunising properties

Vaccination The Reagent Jenner had shown that the cowpox virus maintained its capacity for producing its characteristic lesion and immunity against smallpox when transferred from one person to another and consequently as originally practised vaccination was from 'arm to arm' It was suggested that in this way such diseases as syphilis might be transferred, and *although the Vaccination Commission of 1889–96 con*cluded this could not have happened to any substantial extent that Commission decided that calf lymph should be used for vaccination Accordingly public vaccinators were forbidden by the Vaccination Act of 1898 to employ the arm to arm method Vaccine lymph is now obtained from calves which

have been inoculated with seed lymph This consists generally of strains derived from smallpox passed through monkeys and then on to bovines and by periodical cutaneous passage through the rabbit the capacity of the seed lymph to produce satisfactory vesiculation can be maintained for many years In England the seed lymph is inoculated in calves four to six months old on the abdomen and inner side of the thighs On the fifth day the vesicles are removed by a Volkmann spoon and after trituration glycerine is added and also oil of cloves The lymph is then stored in the cold room below the freezing point of water Before issue it is put up in capillary tubes each containing about $\frac{1}{40}$ c c of emulsion an amount sufficient for one vaccination Also before issue the calf is slaughtered and a thorough post mortem examination made Bacteriological examination of lymph is also carried out and none is issued until organisms are eliminated or reduced to 5 or less per milligram Control of all institutions producing vaccine lymph for sale in this country has been established in Great Britain by the Therapeutic Substances Act 1925 which by means of regulations prescribes standards of potency quality and purity

Whilst calf lymph has a long and honourable career as a remarkably efficient antigen it is hardly to be supposed that immunologists would rest content with a reagent from which contaminating organisms could not be excluded especially in the earlier stages of production New possibilities have arisen since the introduction of culture virus This has been used in human vaccination but while successful takes can be produced the resulting immunity when tested by subsequent vaccination with calf lymph has been shown by Donally (1939) to be much less durable than that obtained by the older method Whether this is due to the intracutaneous method of injection practised or to a diminution of the virulence following artificial culture is not yet clear but while there are inherent possibilities in the use of culture virus it would be unwise in the meantime to supersede the method of calf lymph vaccination by scarification unless for experimental work

Method of Vaccination Inoculation by *scarification* is almost invariably practised in the United Kingdom The site chosen is usually the skin over the insertion of the deltoid but

practitioners are often requested to vaccinate female children or young women on the leg and for this purpose a site about the middle of the external surface of the thigh may be chosen We cannot say however that our experience has always been happy in the choice of this site as the proximity to the napkin area in children and the free movement in adults sometimes results in severe reactions After rendering the skin surgically clean with soap and water or methylated spirit and making sure that it is thoroughly dry afterwards the contents of the capillary tube are expelled in a single drop or divided up into as many drops as insertions Multiple scarification and cross hatching were deprecated by the 1928 Committee on Vaccination which recommended that by means of a needle or scarifying instrument a single scratch about ⅛ inch long should be made through the drop care being taken not to draw blood This procedure seems to have been modified however, as instructions issued with lymph sent out from official sources now recommends scarification to be carried out with three strokes ⅜ inch long and ⅛ inch apart the lymph to be worked into the area of scarification by gentle rubbing with the scarifier We are in agreement with the latter recommendation if for no other reason that the probability of a take is greatly enhanced The lymph should be allowed to dry into the scarified area for at least ten minutes, when a dressing of aseptic lint is put on, and later when the eruption has appeared a mild antiseptic dusting powder may be applied It is unusual for an attempt at primary vaccination to fail provided the operation is carefully performed but if it does, a second and third attempt should be made before accepting the individual concerned as naturally immune to vaccination

Another method is the *multiple pressure* method introduced by Leake and employed in the United States Instead of a simple scratch through the drop of lymph a needle held tangential and parallel to the skin is pressed rapidly into the skin about twenty times the vaccinated area that is the area subjected to pressure from the needle point being kept to the size of 1 or 2 mm It is claimed that this method gives the least amount of trauma and the smallest amount of secondary infection whilst giving the highest percentages of takes and Dudley and May (1932) state that since the introduction of

this method at the Greenwich Hospital the number of days sickness attributed to vaccination has been halved

Inoculation of suitably diluted lymph by *subcutaneous* and *intracutaneous injection* has also been carried out It has been claimed that these methods have the advantage of avoiding a cutaneous lesion and the probability of secondary sepsis but the absence of scar formation as tangible evidence of successful vaccination may be a drawback The work of Henderson and McClean (1939) who employed a bacteria free suspension of vaccinia virus by intradermal injection suggests that a satis factory immunity can only be obtained if a vaccinial vesicle is produced

Clinical Course of Primary Vaccination Evidence of a successful take in primary vaccination is shown by the appear ance of a narrow band of redness along the insertion on the second day whilst on the third day a papule appears On the fourth day the areola increases and the lesion becomes vesicular there being some itchiness and possibly some axillary adenitis From the fifth to the eighth day the vesicles become larger the contents turbid and umbilication may appear During this time *constitutional disturbances* may appear accompanied by pain and stiffness in the shoulder due to swelling of glands in the axilla By the ninth day the lesion becomes pustular the areola broadens and malaise begins to subside The pustule reaches its maximum on the twelfth day central scabbing has become definite and the areola begins to fade On the thirteenth or fourteenth day a firm scab has formed which falls off in two or three weeks leaving a pinkish scar which afterwards becomes pearly white and pitted In addition to various degrees of constitutional reaction and axillary adenitis splenic enlargement with abdominal pain have been recorded in unusual cases *Rashes* may also be found commonly between the ninth and fourteenth day Certain of them are undoubtedly due to cutaneous generalisa tion of the virus and are referred to as *generalised vaccinia* but their occurrence is very rare Jubb (1943) stating that out of 1 025 588 vaccinations 15 cases of generalised vaccinia and 11 doubtful cases were reported to the Government Lymph Establishment while in a further survey 34 cases were found among 3 289 733 vaccinations performed with Government

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Re vaccination As might be expected, according to the interval between primary and re vaccination there are many degrees of reaction to the latter It is convenient however to consider these reactions under three broad headings In the earliest re vaccination which it is possible to assume namely one performed while the successful primary vaccination is in process of evolution a re vaccination may take but its development will be *accelerated* in such a manner that it will reach its climax simultaneously with the primary, and the lesions of re vaccination will be modified Cory (1886) was able to perform successful re vaccinations of this type up till the ninth day of primary vaccination The term accelerated or vaccinoid reaction is also applied to the reaction obtained on re vaccination of subjects who have partial immunity remaining from previous vaccination In this the papular stage appears by the third day and the reaction reaches its maximum by the fifth or seventh day culminating in a small vesicle or papule with scabbing An *immune* reaction has also been described and Leake (1926) states that this is accepted in the U S Public Health Service and Army and Navy as evidence of protection against smallpox It indicates a high degree of immunity and consists of a small area of indurated erythema surrounding the insertion and reaching its maximum on the second or third day Occasionally the reaction may reach the papular stage

Accidental vaccination occasionally occurs in patients with active vaccinia lesions who have brought these in contact with a cut or abrasion in the skin This *auto inoculation* will result in an accelerated reaction Similarly such lesions may infect others *hetero inoculation* in whom the lesions may run an ordinary or accelerated course according to whether the infected person has been previously vaccinated Unless considerable care is exercised auto or hetero inoculation may readily occur and when mass vaccination is being carried out in the presence of an epidemic such lesions may give rise to difficulties in differential diagnosis since morphologically they are the exact counterpart of the individual pocks of variola *When as has occurred in our experience hetero* inoculation takes place on a relatively extensive eczematous surface on the face or hands the similarity to smallpox may

lymph According to Ricketts the distribution of these generalised rashes is more closely akin to chickenpox than smallpox and all lesions are superficial They are sparse commence as small papules become vesicular and finally scab but occasionally abort at the papular stage while some have noted a special prevalence on the vaccinated arm in addition to the trunk Another type of rash seen about the same time is a *non specific eruption* explicable on the basis of sensitivity to the protein in the lymph or of absorption of toxic products from the vaccination lesion Gammie (1944) estimated their occurrence as about 1 800 vaccinations during the Edinburgh outbreak in 1942 Usually they are classified as morbilliform but eruptions of the erythema multiforme and papular urticaria type are well known to occur while scarlatiniform urticarial and various undifferentiated types have been reported

Duration of Immunity Active immunity against smallpox as judged by insusceptibility to re vaccination is commonly acquired on the ninth or tenth day after successful vaccination and the protection so acquired is generally regarded as lasting *for five to ten years although as in all forms of active immunisation* there may be occasional exceptions In the individual it can only be estimated by the reaction to re vaccination but it is of importance to note that a vaccinated person may still *show protection against smallpox although his immunity to* vaccinia as indicated by his capacity to show the dermal reaction to vaccination has completely disappeared and A I Cameron gave it as his opinion in evidence before the *Committee on Vaccination in 1928* that as estimated by protection against death the influence of primary vaccination dating mainly from infancy is not exhausted at the sixtieth year of life That this cannot however be relied on in every individual case was brought out by our experience in Edinburgh in 1942 when four fatal hæmorrhagic cases occurred in patients aged fifty five to fifty nine years all showing vaccination scars dating from infancy Undoubtedly successful re vaccination is a powerful adjuvant of immunity This is shown by the high proportion of those successfully re vaccinated who remain completely insusceptible to further vaccination, and who escape the disease or suffer no more than a minor attack when exposed to smallpox itself

from 1923 onwards of reports of acute nervous disease in association with vaccination This took the form of acute meningo myelo-encephalitis and the condition is now usually referred to as post vaccinial encephalitis although Marsden and Hurst (1932) have suggested the term acute perivascular myelinoclasis as more accurately indicating its essential features The condition claimed the serious attention of all public health workers and some detailed consideration is therefore necessary

Post vaccinial Encephalitis The condition was investigated by a Committee appointed by the Ministry of Health who published reports in 1928 and 1930 and to these we are indebted for much of the following With regard to the epidemiological features a certain geographical and familial incidence of cases was noted Sex distribution was about equal and approximately two thirds of the cases were between the ages of five and fifteen years In nearly all cases the com plication followed primary vaccination with four insertions and in a large proportion it occurred between the seventh and fourteenth day of vaccination From the latter data it was impossible to avoid the conclusion that the process of vaccina tion was responsible for initiating the nervous disturbance The characteristic histo pathological appearance of brain and cord were perivascular demyelination and proliferation of neuroglia infiltration of the perivasular spaces with lympho cytes and intense congestion and hæmorrhage of meningeal vessels No particular batch of lymph was implicated and three hypotheses to account for the condition were considered In the first it was suggested that the complication was due to the action of some neurotropic virus with which vaccination simply happened to coincide secondly that the sequelæ were due solely to the action of vaccinia virus itself and lastly that the onset of the condition was produced by the stimulation into activity by the vaccinia virus of some latent neurotropic virus in the vaccinated subject The last theory was that accepted by the Committee and was supported by the fact that a condition identical pathologically with post vaccinial encephalitis has been described after measles rubella chicken pox smallpox influenza mumps typhoid fever whooping cough and rabies inoculations These occurrences have given

be close The *varicelliform eruption of Kaposi* is now usually attributed to accidental infection with vaccinia virus

Vaccination in Smallpox Ker states that anyone successfully vaccinated within three days of a single exposure to smallpox may be regarded as practically safe from the disease If successful later in the incubation period vaccinia and smallpox may be concurrent but the prognosis of smallpox will be improved Most others who have written on the subject are in agreement with this but that there are exceptions cannot be doubted and these are *sufficiently numerous to necessitate* care in making predictions in individual cases For example we have personal records of three patients successfully vaccinated on the fourteenth thirteenth and eleventh day respectively before the outcrop of the rash and of four others similarly protected on the tenth and ninth days All developed smallpox certainly of the discrete or sparse discrete type so that some modification may have taken place, but complete protection was not obtained In another instance a patient successfully re vaccinated seven days before the true rash appeared contracted a hæmorrhagic attack It would be well therefore to abide by Rickett s view which was that while it was accurate in the main to say that successful vaccination done in the first seven days of exposure would wholly prevent attack there were occasional exceptions to this rule and a patient may be vaccinated as early as the fourteenth or fifteenth day before the outcrop of the rash and yet not escape the disease He also stated that protection against smallpox can never be promised confidently if its acquisition be postponed till after exposure Successful vaccination may be possible throughout the incubation and initial periods of the disease but all are agreed that this is impossible after the third day of the true eruption and a successful vaccination at this stage of a suspected rash rules out smallpox

Complications of Vaccination These are mainly of the septic type such as *cellulitis* *Erysipelas* arising in a vaccination lesion has occasionally been found whilst *tetanus* has been reported in the United States by Clark (1929) as the most important complication of vaccination the use of contaminated bunion pads as dressings often being the cause Of probably greater significance however, was the appearance in Europe

of the complication including 12 deaths were reported. Obviously therefore this grave sequel must always be reckoned with when vaccination requires to be carried out on a large scale, Tait (1943) having estimated during the Edinburgh outbreak in 1942 that it occurred in 1 per 65 808 re-vaccinations and in 1 per 6 332 primary vaccinations.

Administration of Vaccination. The Minister of Health in 1929 gave effect to certain of the recommendations of the Committee on Vaccination, the chief being that public vaccinators were permitted to perform vaccination by *one* linear insertion, whilst primary vaccination at school age and in adolescence was discouraged unless the individuals concerned were actual smallpox contacts. The occurrence of post-vaccinal encephalitis however brought the whole question of compulsory infantile vaccination into prominence, and a strong body of medical opinion has asserted that no harm will follow the repeal of the compulsory clauses in the Vaccination Act, as will result from the Health Services Act 1946. It is concluded that as much vaccination will be carried out in the future as at present, this being secured by the education of the lay public in the same way as immunisation against diphtheria is at present. It is also believed that port sanitary administration is now sufficiently effective to prevent the introduction of smallpox to any great extent, and in any case outbreaks of variola major can soon be brought under control. As might be expected, however, opinion is by no means unanimous and there are many who will regret the abandonment of compulsion. They say that the response to voluntary immunisation against diphtheria has not been enthusiastic in spite of the strenuous propaganda employed during the war years, and that with the disappearance of the statutory obligation the numbers vaccinated will almost reach vanishing point. Moreover, the popularisation of air transport has brought countries in which variola major is epidemic within a few days' journey of the United Kingdom, and this constitutes a potential danger against which compulsory vaccination would provide the only real safeguard.

Efficacy of Vaccination. However much opinion may vary as to vaccination policy, there can be no doubt as to its status as an immunological procedure of the highest value and

weight to the assumption that individuals in whom post infective encephalitis occurs harbour a common virus which becomes activated by various specific infections of which vaccinia is one A number of workers however agree with Jorge (1931) that vaccinia virus is the direct cause of the complication The onset is usually sudden about the tenth or twelfth day after vaccination and is accompanied by pyrexia headache vomiting and drowsiness which may pass quickly into deep coma These are the cardinal signs and symptoms and may be followed by localised paralyses of upper motor neurone type Incontinence is common and convulsions athetosis tremor and choreic movements have all been noted Reflexes are variable but signs of meningeal irritation were present in all cases which have come under our own observation The cerebro spinal fluid obtained on lumbar puncture is under pressure, but is clear and contains an excess of mononuclears whilst an increase in protein is to be expected From one third to one half the cases terminate fatally most of them in the first week death being preceded by coma On the other hand some cases are mild and recovery ensues within the same period When the latter occurs it is complete although in a few cases some mental deterioration and residual paralysis have been noted Improvement has been described *following the intramuscular intravenous and intrathecal* injection of serum from recently vaccinated persons whilst in the United Kingdom a horse anti vaccinial serum is available from the Lister Institute This result would favour the view that the vaccinia virus itself is the responsible agent In Holland the serum of cases convalescent from post vaccinial encephalitis has been employed but such a serum would obviously be very difficult to obtain in an emergency Our own experiences with the intramuscular injection of whole blood from recently vaccinated persons in a small series of patients do not indicate that much is to be expected from this line of treatment *In spite of the modifications in the technique* and administration of vaccination following the Reports of the Vaccination Committee cases of post vaccinial encephalitis have continued to occur and during the mass vaccination carried out in Scotland in 1942 when approximately 925 000 persons submitted themselves to the operation 34 instances

CHAPTER XII

MUMPS

Synonym—Epidemic parotitis

Pathology Several workers have been able to reproduce various manifestations of mumps in animals and Johnson and Goodpasture (1934 1935) have shown conclusively that the cause of the disease is a filterable virus which was successfully transmitted by injection of saliva from human cases into the Stenson s duct of monkeys After passage through monkeys the virus on inoculation into human volunteers again produced mumps In the natural infection in man the chief local effect is on the salivary glands but that there is a generalised distribution of the virus is evident from the inflammatory reaction which occurs in a proportion of cases in such glands as the testis pancreas and in the cerebro spinal fluid Histologically parotid glands from cases of mumps in man and the experimental condition in monkeys show parenchymatous degeneration and mononuclear infiltration The blood picture in mumps is constant and from the onset there is a leucocytosis with a relative lymphocytosis

Etiology Mumps has a universal distribution and according to Gundersen (1934) who has studied the disease in Norway epidemic prevalence begins in the autumn reaches its maximum in January and February dies down in spring and practically disappears in summer The commonest age incidence is between five and fifteen years especially in the latter part of that age period but adults living in isolated communities are readily infected on exposure Sex incidence also according to Gundersen is equal at the commonest age period but after that he found twice as many males as females affected Mortality is negligible and it is believed that the deaths registered as resulting from mumps include a proportion which are probably due to other causes

Transmission The virus being contained in saliva transmission is entirely by direct contact and droplet spray infection gaining entrance into the mouth and nasopharynx

indeed in this respect it stands pre-eminent as a method of active immunisation There is an enormous literature on this subject and much of the statistical data has withstood the searching analysis of the modern statistician Thus Greenwood (1934) infers from the statistical evidence that "Jenner was directly or indirectly the means of saving many hundreds of thousands of lives" The main facts are summarised by Newman who referring to variola major states that it is

beyond all question that the mortality of smallpox is much less than in pre vaccination times that the greatest diminution in the smallpox mortality is found in the earlier years of life in which there is most vaccination that in countries where there is adequate vaccination and re vaccination relatively to the population there is little smallpox and that the fatality rate among persons attacked by smallpox is much greater, age for age among the unvaccinated than the vaccinated



Fig. 60. Unilateral mumps showing enlargement of left parotid, which can be compared with normal right side of face.

Infectivity Mumps may spread comparatively widely in communities containing children and adults unprotected by previous attacks Thus Kelly and Reite (1934) found that over 26 per cent of non immune family contacts contracted the disease on exposure and this is similar to Gundersen s experience in the general population during epidemics in Norway The disease is much less infectious however than measles and chickenpox and in ward outbreaks when the primary case is promptly isolated further cases are often avoided Moreover we have found that cases of mumps can be successfully isolated by bed isolation methods at all stages of the disease The patient is probably capable of spreading infection from the first symptom until the swelling of the salivary glands has subsided

Incubation and Quarantine Periods The maximum limits are given as from twelve to twenty eight days but secondary cases occur commonly from the seventeenth to the twentieth A quarantine period of twenty eight days is generally recommended

Clinical Features of the Disease Before the nature of the condition discloses itself a preliminary period of a day or two of malaise headache sore throat and fever occasionally may be found Usually however these symptoms appear about *the same time as the parotid swelling which as a rule is uni* lateral at first The enlargement can be seen below the ear and behind the angle of the jaw as it becomes more pronounced forming a bulge on the cheek in front of the ear the most prominent part being about the level of the lobe The swelling is tender and causes pain and difficulty on opening the mouth the overlying skin, though retaining its normal appearance usually being more or less tense The specific reaction may also occur in the submaxillary and sublingual glands on the same side, and, within three or four days the parotid, *or* a little later the salivary glands on the other side may *also be implicated* There is a great amount of variation in glandular swelling, from slight enlargement of one parotid to massive enlargement of both parotids submaxillaries and sublinguals extending down to the clavicles but examples of the latter degree of involvement are not common In addition to inflammation of the salivary glands there is congestion of the

fauces or even tonsillitis and possibly redness and œdema of the orifice of Stenson's duct. Suppuration in the parotids although it does occur is very rare, the glands undergoing resolution in from three or four to ten days, but in severe cases they may take two or three weeks to subside. *Constitutional disturbances* vary according to the amount of glandular enlargement. Thus they may be slight, with a mild fever terminating a day or two before the complete disappearance of the swelling. On the other hand, when the glandular inflammation is extensive or prolonged, the temperature remains between 100° and 103° F for a week or longer, and this may be accompanied by a considerable degree of prostration from which the patient may take two or three weeks to recover. In the majority of cases convalescence is uneventful, but at the end of the first or beginning of the second week *orchitis* may supervene in males. This occurs in about one fifth of all cases in males above puberty, and whilst commonly unilateral may be bilateral. The condition is usually ushered in by rigors, vomiting, sudden elevation of temperature, and sometimes delirium. The testis is swollen, tender and dragging pain is complained of, whilst the skin may show a dusky redness. Recovery takes place in from a few days to a week, but all agree that atrophy is not an uncommon sequel, and Stengel (1936) estimates that a relative or temporary degree occurs in 40 to 60 per cent of cases. The pancreas may also be affected, *acute pancreatitis* showing itself in the second week by the sudden onset of epigastric pain, vomiting, pyrexia and collapse, the condition subsiding in a few days. Death following this condition has been reported, whilst a permanent glycosuria following mumps without evidence of intercurrent pancreatitis has been described by Dick (1933). Other glands

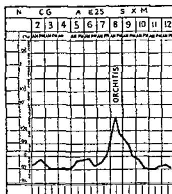


FIG 61 Temperature chart of mumps showing orchitis commencing on eighth day. Note absence of pyrexia on second to the sixth days during which parotitis was present

be often left out of the clinical picture the only manifestations of the disease being submaxillary or sublingual adenitis or even orchitis and in such cases the finding of the typical lymphocytosis on examination of the blood will be helpful especially if a history of exposure to mumps can be obtained A parotitis usually unilateral may occur in enteric and after acute abdominal conditions and abdominal operations but these usually suppurate and if the primary disease be the result of a septic process polymorph leucocytes will predominate in the blood picture A most serious mistake is to regard severe nasopharyngeal diphtheria as mumps but even a cursory examination of the throat should prevent this error The adenitis of scarlet fever may suggest mumps but a little observation should usually clear up the diagnosis Glandular fever will occasionally be mistaken for mumps but Tidy (1934) states that in this condition the parotid is never affected

Prognosis This is almost invariably favourable as far as recovery is concerned the main practical point requiring consideration being in connection with the future activity of the testis when orchitis has occurred As we have seen atrophy occurs in a fairly high proportion of cases but it would appear to be usually only partial In the unusual event of the occurrence of pancreatitis the possibility of subsequent glycosuria should be remembered and if otitis interna appears permanent deafness will result Death may result from meningo-encephalitis although according to Johannsen (1930) recovery almost always takes place

Prophylaxis Prompt isolation will do something to prevent spread whilst school contacts are usually excluded from school for a month Attempts to secure passive immunisation by means of convalescent mumps serum have only resulted in partial success so far

Treatment At the outset of the disease the patient should be isolated in bed and a brisk aperient given Careful attention should be given to the toilet of the mouth as long as the parotid swelling is present and owing to the difficulty in mastication nourishment will require to be restricted to nourishing fluids ice cream junket and jellies For simple parotid swelling warm wool and a bandage may be sufficient local treatment but if there is much pain and swelling hot

which have been recognised as the seat of inflammation are the *ovaries* and the *breasts* *Meningo encephalitis*, often referred to as mumps meningitis, as a clinically demonstrable condition is comparatively rare but the old standing observation that latent involvement of the central nervous system is common has received confirmation by a number of modern workers For example Holford (1934) found that routine lumbar puncture during mumps almost invariably shows a rise of intraspinal pressure and pleocytosis even in the absence of signs or symptoms suggestive of abnormality When meningo-encephalitis declares itself clinically it may occur before simultaneously with or after the parotitis or other manifestation of mumps such as orchitis and that it has an etiological relationship with the causal virus has been shown by Jersild (1942) who reported it in a mumps epidemic as the sole manifestation of the disease in close contacts The onset of the condition is indicated by headache vomiting pyrexia drowsiness and signs of meningeal irritation whilst the cerebro spinal fluid obtained on lumbar puncture is under heightened pressure shows an excess of lymphocytes and contains increased protein Ordinarily it lasts for several days and settles without residual phenomena Fatal cases have occurred however and neurohistological examination of these *has shown characteristics similar to those in the group of* post infectious encephalitis found after many common infectious diseases

Relapse and Second Attack Relapse accompanied by return of swelling in one or both parotids may occur when resolution is taking place, or even when it has been completed but this is very rare as also are second attacks of the disease

Complications A great variety of conditions occurring in convalescence have been described as complications of mumps but there are not many which appear sufficiently constantly to warrant their being regarded as true complications Acute otitis media has been noted in some outbreaks whilst otitis interna although very uncommon is usually regarded as having a specific relationship to mumps

Diagnosis There is usually little difficulty in making the diagnosis the typical swelling of the face being unmistakable It should be remembered however, that parotid swelling may

be often left out of the clinical picture the only manifestations of the disease being submaxillary or sublingual adenitis or even orchitis and in such cases the finding of the typical lymphocytosis on examination of the blood will be helpful especially if a history of exposure to mumps can be obtained A parotitis usually unilateral may occur in enteric and after acute abdominal conditions and abdominal operations but these usually suppurate and if the primary disease be the result of a septic process polymorph leucocytes will predominate in the blood picture A most serious mistake is to regard severe nasopharyngeal diphtheria as mumps but even a cursory examination of the throat should prevent this error The adenitis of scarlet fever may suggest mumps but a little observation should usually clear up the diagnosis Glandular fever will occasionally be mistaken for mumps but Tidy (1934) states that in this condition the parotid is never affected

Prognosis This is almost invariably favourable as far as recovery is concerned the main practical point requiring consideration being in connection with the future activity of the testis when orchitis has occurred As we have seen atrophy occurs in a fairly high proportion of cases but it would appear to be usually only partial In the unusual event of the occurrence of pancreatitis the possibility of subsequent glycosuria should be remembered and if otitis interna appears permanent deafness will result Death may result from meningo-encephalitis although according to Johannsen (1930), recovery almost always takes place

Prophylaxis Prompt isolation will do something to prevent spread whilst school contacts are usually excluded from school for a month Attempts to secure passive immunisation by means of *convalescent mumps serum* have only resulted in partial success so far

Treatment At the outset of the disease the patient should be isolated in bed and a brisk aperient given Careful attention should be given to the toilet of the mouth as long as the parotid swelling is present and owing to the difficulty in mastication nourishment will require to be restricted to nourishing fluids ice cream junket and jellies For simple parotid swelling warm wool and a bandage may be sufficient local treatment but if there is much pain and swelling hot

fomentations or poultices will be necessary. In orchitis a supporting bandage with lead and opium lotion should be applied, and if pain is very severe morphia is required. In severe cases with considerable swelling orchidectomy has been recommended and while some have doubted whether this is necessary in a condition which will clear up in a matter of days McGuinness and Gall (1944) found that the operation gave considerable relief from pain and consider that it is justifiable to suggest it on the second testicle as soon as involvement is recognised and in cases of severe unilateral orchitis. In pancreatitis the patient is given frequent small feeds of milk and heat applied to the abdomen. Pilocarpine and lumbar puncture have been recommended for otitis interna and in serous meningitis and encephalomyelitis lumbar puncture should be repeated as long as signs of meningeal irritation persist. In view of the possibility of glandular metastasis especially the occurrence of orchitis in males the patient should remain in bed for at least ten days. Isolation should be maintained during this period or until swelling of the salivary glands has subsided.

CHAPTER XIII

RUBELLA

Synonyms—German measles rose rash rotheln

Pathology The causal agent of rubella has not been identified but from the general characteristics of the disease it has been assumed to be a virus From the clinical stand point and particularly in respect of *diagnosis* the most important pathological changes are in the blood According to Hynes (1940) there is a leucopenia at first but the leucocyte count rises to the upper limit of normal by the tenth day Turck cells are always present are commonly numerous and reach their maximum about the fourth day Plasma cells are present in from a half to a third of the blood of patients in the first week of the disease

Etiology Rubella occurs in all quarters of the globe and in the United Kingdom assumes epidemic prevalence in the spring and summer months Statistics of age incidence being mostly compiled from selected hospital cases show much variation but the maximum age incidence falls later in life than measles and young adults not infrequently contract the disease It is outstanding among the common infections in that it shows but little morbidity and no mortality although the observations of Gregg and others would appear to indicate that it is not quite the trivial infection it was presumed to be in the past

Transmission The disease spreads from case to case by droplet infection inhaled by the infected person

Infectivity When the disease occurs among children or young adults especially in closed communities secondary cases are almost inevitable but nevertheless we have found that spread can be prevented by barrier nursing infectivity thus being less than in measles or chickenpox Infectivity is greatest in the early catarrhal stage and disappears with the rash

Incubation and Quarantine Period The limits of the incuba tion period may be given as from ten to twenty-one days the

bulk of cases occurring between the fourteenth and eighteenth days If a quarantine period is prescribed for contacts twenty one days would be adequate

Clinical Features of the Disease An invasion period of two or three days may be noted and premonitory symptoms may even be present for as long as a week During this time the patient suffers from malaise and some headache but the most characteristic features are slight coryza and sore throat associated with stiffness of the neck due to inflammation of the lymph nodes in the posterior triangle Often however attention is first drawn to the case by the appearance of the rash which is not long preceded by catarrhal symptoms The rash is seen on the brow covers the whole of the face and quickly spreads over the whole body It is macular in character and in an average case the spots tend to remain discrete the intervening skin retaining its normal appearance, although in some cases the density of the rash is such that a scarlatiniform appearance is presented on the trunk It fades from above downwards and by the time the body and limbs are involved the rash may have disappeared or only show faint traces on the face In general the rash may be expected to retain its distinctive features on some part of the body for one or two days but on the other hand it may be very transient In addition to the rash a varying amount of pink eye and slight faucial congestion may be found Apart from catarrh and possibly slight cough, constitutional disturbances are not severe although on occasion we have noted quite sharp febrile reactions In general however the temperature is raised to 100° or 101° F for about twenty four hours and discomfort may arise from enlargement of glands in the neck part of a generalised adenitis which occurs in a large proportion of cases The inflamed glands vary in size from a lentil to a bean remain firm and discrete and gradually disappear with or shortly after the rash Those which may be affected are the suboccipital post auricular pre auricular post cervical clavicular, axillary epitrochlear and inguinal groups and while any combination may be found the post cervical are most constantly involved With the fall in temperature and resolution of the adenitis the disease is at an end probably not having caused more than a slight upset for a day or two As

a rule complications are unknown but in young adults we have seen relatively sharp attacks with pronounced catarrh followed by a short lived *arthritis* at the end of a week In character and distribution the latter resembled the early arthritis of scarlet fever Of recent years various observers have reported a mild form of *encephalomyelitis* as a sequel to rubella Also attention has been drawn to the occurrence of *congenital defects* in babies born of mothers suffering from the disease in the early stages of pregnancy congenital cataract having been reported by Gregg (1941) and cataract deaf mutism heart disease microcephaly and mental retardation by Swan and others (1943) Relapse and second attack are practically unknown

Diagnosis Since rubella in the great majority of cases amounts to no more than an uncomplicated temporary indisposition its main interest for the practitioner is in respect of diagnosis When occurring in typical form in epidemics with macular rash coryza and generalised adenitis the disease presents little difficulty in diagnosis but the rapid evolution and fading of the rash on the face and possibly on other parts of the body before the case is seen on occasion make the diagnosis somewhat speculative After the rash has gone from the face it may be profuse on the body and simulate *scarlet fever* especially the mild type in which throat signs are poorly marked and tongue changes equivocal On the limbs however the macular character of the rash will often be retained whilst a history of sneezing or other sign of coryza is usually absent in scarlet fever In such cases the absence of blanching when the Schultz Charlton test is performed may be of assistance The characteristic adenitis of rubella is helpful especially when the post auricular sub-occipital and post cervical nodes are enlarged but in attaching evidential value to these it is wise to keep in mind the warning of F H Thomson namely that the enlargement of these glands is valueless from the point of view of diagnosis unless the head is free from vermin and nits and that it is free should never be assumed In certain cases it may be necessary to retain the case under observation and await the appearance of desquamation or typical complications The other main difficulty is with *measles* In the latter the patient as a rule is

more sharply ill and constitutional reaction more profound The catarrh is more severe whilst the presence of Koplik's spots would be decisive The measles rash is much more blotchy and definitely papular, it is seldom short-lived and leaves staining but on the other hand in mild measles and in the attenuated form with which we are now familiar since the introduction of reagents for passive immunisation the individual elements of the rash may remain fairly discrete In such cases the characteristic adenitis of rubella may assist in making the distinction Another specific exanthem *erythema infectiosum*, may be mistaken for rubella In this condition the reticular character of the rash and its predilection for the face extremities and less commonly on the flanks form the most reliable guide to diagnosis *Glandular fever* with a macular rash which occasionally accompanies the onset has been mistaken in its early stages for rubella but the more sustained febrile reaction together with the well marked constitutional effects will indicate that a more severe condition is present A positive agglutination when the Paul Bunnell test is performed will be decisive in favour of glandular fever Various other erythemata resulting from *foodstuffs serum injections* and *dentition* may be confused with rubella but in these coryza is absent and careful examination may reveal urticarial patches which will exclude rubella Various *drug* rashes may simulate rubella more or less closely and among these we have found certain sulphapyridine rashes giving a very good imitation of the exanthem

As has been indicated previously much information can be obtained from an examination of the white blood cells A leucocyte count should be sufficient to distinguish between rubella and scarlet fever the latter showing an initial leucocytosis Apart from clinical differences and the evidence derived from the Paul Bunnell reaction the characteristic blood picture obtained in glandular fever should in itself serve to distinguish between this and rubella Unfortunately blood examination gives no assistance in the differential diagnosis of measles and rubella

Prophylaxis No special measures are carried out for the prevention of this disease except that known contacts should be under observation for three weeks so that they may be

isolated on the first sign of catarrh or rash In view of the occurrence of congenital defects in the offspring every effort should be made to safeguard pregnant women especially during the early stages from contact with the disease

Treatment The patient should be isolated and confined to bed if pyrexia is present During the febrile period a light diet is prescribed and isolation may be terminated when the rash has faded

CHAPTER XIV

ERYTHEMA INFECTIOSUM

Limited outbreaks of this disease also known as Megalerythema Epidemicum and Fifth Disease have been reported in Europe America and China and we agree with J D Rolleston that it is also to be found in the United Kingdom From time to time sporadic cases and groups of cases in families have come under our own observation in Edinburgh and London and we have no doubt that it is a specific infectious disease It occurs chiefly in children between five and fifteen years of age in the spring and early summer months The *incubation period is from four to fourteen days but usually* about a week and the main characteristic of the disease is the rash This commences on the cheeks producing a butterfly pattern of intense uniform erythema consisting of confluent macules In the course of a few hours the rash appears on the prominence of the shoulder spreads from the upper arm chiefly on the extensor aspect and finally involves the whole of the forearm and the dorsum of the hand About this time also it may be seen on the flanks Shortly after the rash is *seen on the upper arm it is found on the buttocks and passes* to the lateral aspect of the thigh the lower leg and the dorsum of the foot The rash at first consists of discrete macules but these fade in the centre so that rings are formed and impinge on each other to form a lacelike or reticular pattern The rash disappears in the order in which it comes out generally remaining visible for two or three days although we have noted one or two cases in which it lasted about a fortnight, the rash disappearing for hours together but capable of being *revived by the application of hot water bottles* Febrile disturbances are mild or absent and there are no complications The disease is of little more than academic importance but is some interest from the point of view of diagnosis all the cases coming under our notice having been sent into hospital as scarlet fever measles or rubella



Fig. 6 Eruption of erythema infectiosum on forearm

[To face p. 60]

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CHAPTER XV

SERUM REACTIONS

Definition As a direct result of the injection of serum for therapeutic and prophylactic purposes reactions are encountered in a proportion of individuals These have been probably mo t extensively studied in connection with diphtheria antitoxin but since they are caused by the introduction into the human subject of a heterologous protein usually that of the horse and have no relationship to the antibody for which the serum forms a vehicle the same clinical features will be found whether they occur in the course of specific treatment for diphtheria scarlet fever or for the prophylaxis or treatment of any disease in which serum is employed The term serum sickness or serum disease has been traditionally employed in referring generally to these reactions but for convenience of description we propose to classify the three main types of reaction into *serum sickness serum shock* and *anaphylaxis* The manifestation known as the Arthus phenomenon is of insufficient practical importance in man to require mention whilst the occurrence of abscesses at the site of injection with the possible exception of their appearance when serum injections are given in the course of generalised blood infection can be ascribed to failure in securing asepsis when performing the injection

Serum Sickness Comprised within the definition of this condition are the sequelæ of injection which supervene after a latent period usually of several days and among which urgent constitutional effects such as rigor collapse and respiratory distress are absent The mechanism by which it is produced is imperfectly understood and according to Mackenzie and Hanger (1930) about 10 per cent of human beings are insusceptible With the dosage of concentrated serum outlined as appropriate in preceding pages for diphtheria, Hilda Davis (1938) in a study of 4 835 serum treated cases at the North Western Hospital from 1929 to 1933 found that generalised serum reactions occurred in 17 5 per cent of patients In

Fig 63 Profuse urticarial serum rash on buttocks and posterior part of thighs following the injection of diphtheria antitoxin



Fig 64 Morbilliform serum rash after injection of diphtheria antitoxin

scarlet fever The age of the patient and the route of injection would appear to have little effect on incidence

The *latent period* between serum administration and the appearance of signs of serum sickness may be anything between six to fourteen days but nearly half the cases group themselves within an eight to ten day period The commonest and sometimes the only manifestation is *rash* This often commences at the site of injection and remains *localised* to that site covering a few square inches of skin without other signs or symptoms Such rashes may take any of the forms hereunder described in connection with serum sickness but one type is of particular interest an erysipelatoid patch centred on the point of inoculation which may be mistaken for true erysipelas This result of serum injection is usually classified as a local reaction and is not usually regarded as serum sickness for statistical purposes though obviously of the same nature The *generalised* serum rash assumes an irregular distribution over the body with a well recognised tendency to come and go In type it is nearly always urticarial and often itchy to the point of discomfort or even misery to the patient Occasionally the rash may be circinate scarlatiniform or morbilliform sometimes a formless patchy erythema or again all these elements may be present Purpuric rashes are rare and we have seen them in only two instances Other manifestations are found in probably less than 5 per cent of cases of serum sickness Of these *pyrexia* is most often noted usually between 100 and 102° F *Arthritis* and *myalgia* localised *œdema* of face genitals and extremities temporary *albuminuria nausea* and *vomiting adenitis* of the lymph glands draining the area of injection are also to be found and indeed any of these may be the sole indication of serum sickness Enlargement of spleen and neurological complications are extremely rare This description applies to serum sickness as occurring after the administration of concentrated serum It seldom lasts more than twenty four hours and indeed may be very transient Following the use of the unconcentrated product the manifestations are much more severe and marked by considerable pyrexia and constitutional disturbance Rashes tend to be heavy lasting a few days to a week whilst secondary and even tertiary rashes may appear subsequently Arthritis and

serum treated cases of scarlet fever in which a high proportion of the patients received 10 c c of concentrated scarlet fever antitoxin, our experience has been that 25 to 30 per cent will show generalised reactions whilst with the serum formerly employed in the treatment of cerebro spinal meningitis reactions occurred in 80 to 90 per cent *There can be no* doubt that the most important factor in the causation of serum sickness is *sensitisation* as the result of previous serum injection Davis found in serum treated diphtheria patients that in those with a history of serum injection on a previous occasion on receiving 8 000 units or less 27 9 per cent developed serum reactions, between 8 000 and 24 000 units 49 5 per cent and over 24 000 units 66 7 per cent Next in importance to sensitisation from previous injection is the *quantity* of foreign *protein injected patients receiving small amounts showing* a low incidence and mild attacks of the condition and in those to whom relatively large amounts are administered a less number escape and the reactions are sharper This is well brought out by Davis analysis which shows that in those receiving 8 000 units or less of diphtheria antitoxin 5 1 per cent contracted general serum reactions in those receiving 8 000–24 000 units the incidence was 31 7 per cent, and in those who received over 24 000 units the incidence was 36 0 per cent *For the same reason unconcentrated serum gives a* much higher proportion of cases and a more severe type of serum sickness than the concentrated from which much of the inert protein has been removed This was shown at the North Western Hospital in the period 1925–27, the percentage incidence of serum sickness in diphtheria patients falling from 44 3 per cent to 15 7 per cent when unconcentrated was replaced by concentrated antitoxin the average unit dosage per patient remaining approximately the same Within the past *few years a further refinement in serum production has* been brought about in the removal of inert proteins by a process of controlled digestion with proteolytic enzymes In addition to permitting the injection of much larger doses of antibody in smaller bulk the introduction of this refined and concentrated serum has reduced the incidence of serum sickness in all cases of diphtheria to about 5 per cent in our experience whilst there has also been an appreciable reduction in serum treated cases of

of inorganic substances we are inclined to attribute their occurrence to the route rather than the nature of the reagent The most frequent manifestation is chill but this may be pronounced so that rigors accompanied by collapse occur Although alarming the patient rapidly recovers and much can be done to minimise the effects by making sure that the patient is thoroughly warm in bed before commencing the injection raising the foot of the bed and injecting the serum slowly at body temperature whilst a hypodermic syringe and adrenalin should always be at hand when intravenous injections are given If shivering begins during the process of injection this should be discontinued immediately The tendency to serum shock can also be averted by giving the serum intra venously by the drip method in one or two pints of 5 per cent glucose in saline kept at body temperature

Anaphylaxis This term refers to the sudden and occasion ally fatal reactions which in rare instances have been associated with injections of even minimal amounts of serum by the subcutaneous route Its frequency in the human subject has been estimated by Park (1908) to be about twice in 50 000 serum treated cases and those in whom the phenomenon has been observed fall into two groups viz individuals naturally sensitive to horse protein and those who have been sensitised as a result of previous serum injection The former group has provided most of the authenticated cases the subjects being sensitive to such small amounts as 0 5 c c of serum given subcutaneously and frequently giving a history of asthma or some allergic manifestation In the group previously sensitised by serum few appear to reach a dangerous degree of sensitisa tion the most usual reaction being an ordinary attack of serum sickness of the accelerated type described above Anaphylaxis is characterised by sudden *collapse* and marked *respiratory distress* with laboured breathing and coughing *frothy expectoration cyanosis rigors* fleeting *erythematous rashes* and localised *œdema* Immediate energetic treatment as for shock is necessary and adrenalin should be pushed With a view to prevention it should be the unvarying rule to ascertain the history of all patients to whom it may be necessary to administer serum in respect of such conditions as previous serum injection asthma or hay fever In the event of such a

myalgia are more frequent and distressing whilst œdema and marked albuminuria are often prominent Such reactions after the employment of unconcentrated serum are now largely of historical interest as few therapeutic sera now in common use are unconcentrated but their character may serve to explain our predecessors occasional hesitance in giving serum In view of the obvious advantages which refined and concentrated serum has over the unconcentrated we recommend unhesitatingly the former for the treatment of any disease which is susceptible to serum therapy It is true that Abt (1922) suggested that in the case of diphtheria the combining *power of unconcentrated antitoxin for toxin is superior to that* of the concentrated but convincing experimental or clinical evidence has never been adduced in favour of this and the tendency of modern laboratory workers has been to seek improved methods of refinement and concentration so that sera of higher potency may be obtained *Accelerated reactions* are seen in those who have previously been the recipients of serum They do not differ in type from serum sickness as ordinarily observed except that the latent period is reduced from one to seven days over 60 per cent according to Davis occurring between the fifth and seventh days Whilst occasionally producing severe discomfort serum sickness has rarely been known to be dangerous and complete recovery is the rule in the course of a day or two *Treatment* consists in the application of calamine or sodium bicarbonate lotion to the skin Aspirin will probably allay the general discomfort in the ordinary case but if the rash is very irritating or persistent hypodermic injections of adrenalin 1 in 1 000 in 0 5 or 1 0 c c doses often have a striking effect Only very infrequently will *the practitioner be compelled to prescribe morphia to alleviate* the intolerable irritation of severe eruptions which fail to yield to adrenalin

Serum Shock This form of serum reaction has also been designated *immediate thermal or anaphylactoid* reaction It is encountered *during or within half an hour to two* hours after intravenous injection of serum usually in large amounts Minor degrees of this condition will be observed in a fair proportion of patients receiving serum in this way and since a similar condition is found after the intravenous injection

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history being forthcoming desensitisation should be attempted To prevent anaphylactic accidents many efforts have been made to devise a satisfactory test for the detection of hyper sensitive individuals These have taken the form of intra cutaneous *injections or conjunctival instillations of diluted* serum, but the reactions produced are uncertain guides to the subsequent results of serum administration and it is doubtful if at present their routine application has any practical advantage

Desensitisation Whilst on theoretical grounds it is doubtful if desensitisation of the human subject is possible cases will be encountered which have previously been injected with serum or have a history of some allergic manifestation and in which it is necessary to attempt serum administration The procedure recommended by the L C C Departmental Committee on Antitoxin Dosage (1936) is that cases which give a history of previous serum administration should have a preliminary injection of 0 5 c c of the therapeutic serum subcutaneously If no reaction occurs within half an hour then the full therapeutic dose should be given by the appro priate route If a reaction does occur, the dose of 0 5 c c should be repeated subcutaneously at intervals of not less than half an hour until the reaction is minimal, the remainder of the required dose being then given intramuscularly In cases which present a history of asthma or allied conditions, or of reaction to previous serum administration the procedure is more elaborate The attempt at desensitisation is begun by the subcutaneous injection of 0 2 c c of a 1 in 10 dilution of *the therapeutic serum* in saline If no reaction occurs within half an hour 0 5 c c is given intramuscularly, and if again no reaction occurs the full dose should be given intramuscularly *In asthmatics the intravenous route should be avoided* Should a reaction occur at one or other of the preliminary injections, the dose should be fractioned in amounts of 0 2 to 0 5 c c and given cautiously at half hourly intervals by the subcutaneous route When the reaction becomes minimal a small dose should be given intramuscularly before adminis tering the remainder by this route For those known to be highly sensitive sera made in animals other than the horse *e g* the goat should be considered

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